

3rd Annual Green Chemistry and Engineering Conference Proceedings

Moving Toward Industrial Ecology

June 29–July 1, 1999
Washington, D.C.

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Proceedings

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1999 Green Chemistry and Engineering Conference
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**ENVIRONMENTALLY
BENIGN SYNTHESIS**

NONCLASSICAL ENERGIES AS SOURCE FOR SUSTAINABLE ORGANIC REACTIONS

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Introduction

Population growth and rising living standards in the industrial countries, as well as an expansion of the market economies, necessitate an increase in production and consumption.

Natural resources for the production of goods are taken from the environment. Wastes and contaminants from production processes are discharged into the environment. As a result the environment is exposed to a global impact and endangered: "Sustainable development meets the needs of the present without compromising the ability of future generations to meet their own needs!" (Brundtland Commission)

Sustainability in the economic sense means the efficient allocation of scarce goods and resources. Sustainability in the environmental sense means not to exceed the limits of environmental impact and to maintain the natural basis of life. Sustainability in the social sense means a maximum of equality of opportunity, social justice and freedom. All these three elements must be in equilibrium with each other.

The chemical industry can contribute significantly to this guiding principle. Its contribution is based on the use of environmental protection technologies. While Europe uses this word, America deals with green chemistry!

Why?

The background and the content are the same, but the colour "green" could be misunderstood in Germany. In German politics, parties are commonly named by different colours, for example, the black, the red, the green, the brown, the yellow party, and, of course, red-green or black-red and further alliance.

Okay, but what means Green Chemistry?

"Green Chemistry is the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products" (Anastas, Warner (1998)). Special tools of this "benign of design" are:

- W** Alternative Feedstocks
- W** Alternative Reagents
- W** Alternative Solvents
- W** Alternative Products
- W** Alternative Catalysts
- W** Alternative Energy Stimulants.

We have been dealing with these tools in research and development for three years. Here we report on alternative energy stimulants.

Alternative energy stimulants or non-classical energies have been used — or have been reported to have been used — for many years to increase the reactions rate and to enhance the yield of particular reaction products. We will review the situation in the field of energies and report on own illustrative examples. Non-classical energies lead to innovative methods and techniques for chemical transformations and material separations. Non-classical energies are:

Supercritical Conditions

The application of "high pressures" and "high temperatures" (HP-HT) can lead to new separation technologies, nonorganic solvent processes, milder reaction regimes, improved transport phenomena, higher turnover numbers in heterogeneous catalytic systems, improved hazardous waste treatment processes, and improved solubilities.

Ultrasonic

Based on the phenomenon of cavitation the use of sonowaves can accelerate chemical transformation, affect product distribution, initiate free radical formation and (de)polymerization, induce mechanical cleavage of polymers, increase catalytic activity of metal particles by factors as large as 10^5 . The sonication of organic solutions of metal carbonyls leads to the formation of micro- to nano-particles of metals, alloys, oxides, and semiconductors. Applications in the synthesis of organic fine chemicals are numerous, especially in free radical reactions. Polymer science also has a strong interest in this field.

Microwaves

Microwave radiation can accelerate chemical transformations in solution as well as in solid phase. High yields of highly pure products are reached within a short time. The aim is to search for a specific microwave effect and to scale up the reactions. The choice of solvent controls the dissipative energy transfer. Moreover, it is not always necessary to work in presence of solvent, and this aspect is important for industry.

Plasma

The application of plasma-discharges offers new possibilities for the synthesis of new materials, the treatment of hazardous and toxic waste, and the acceleration of radical induced chemical transformations.

Tribochemistry

The use of mechanical activation is successfully used to carry out some inorganic and organic reactions. Naturally, the rates of the processes greatly depend on the conditions of mechanical load and hence on the design of mechanical activators. The best results are obtained using planetary centrifugal mills with acceleration factors of 50-100 g and an $1\text{-}10^3$ g charge of the material treated.

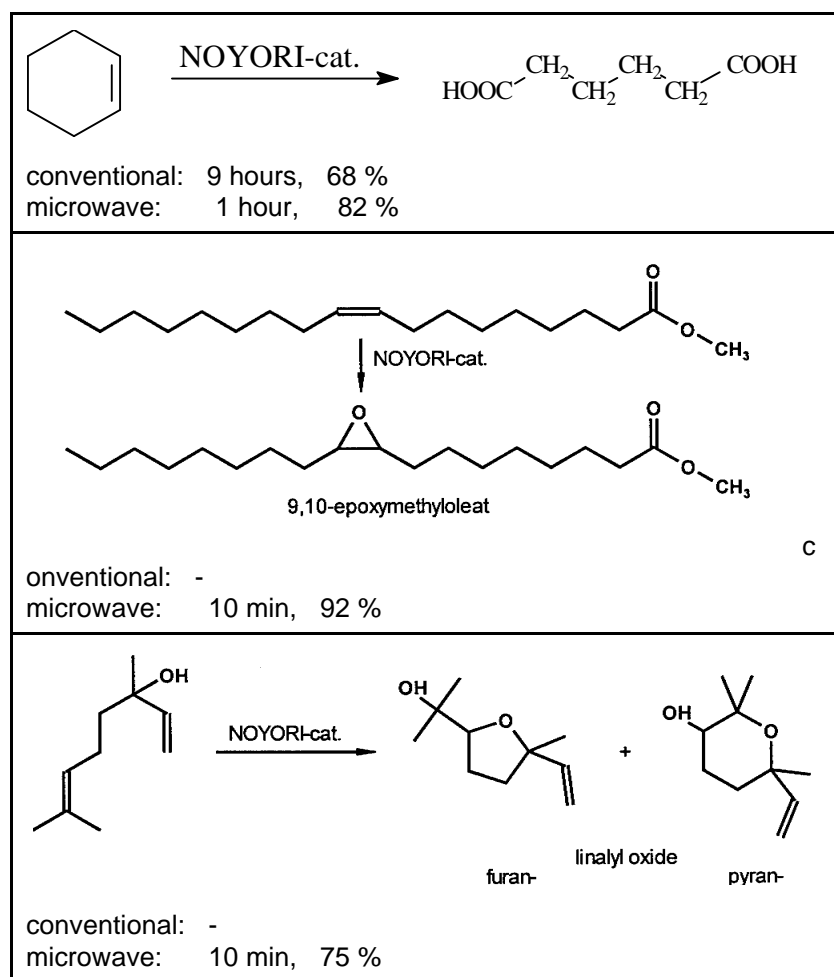
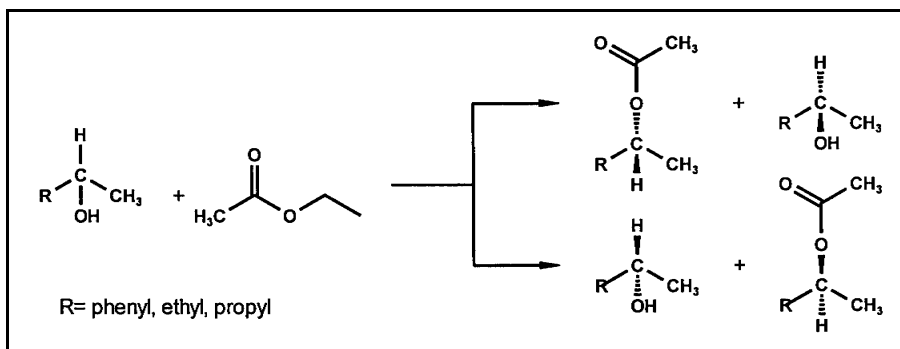


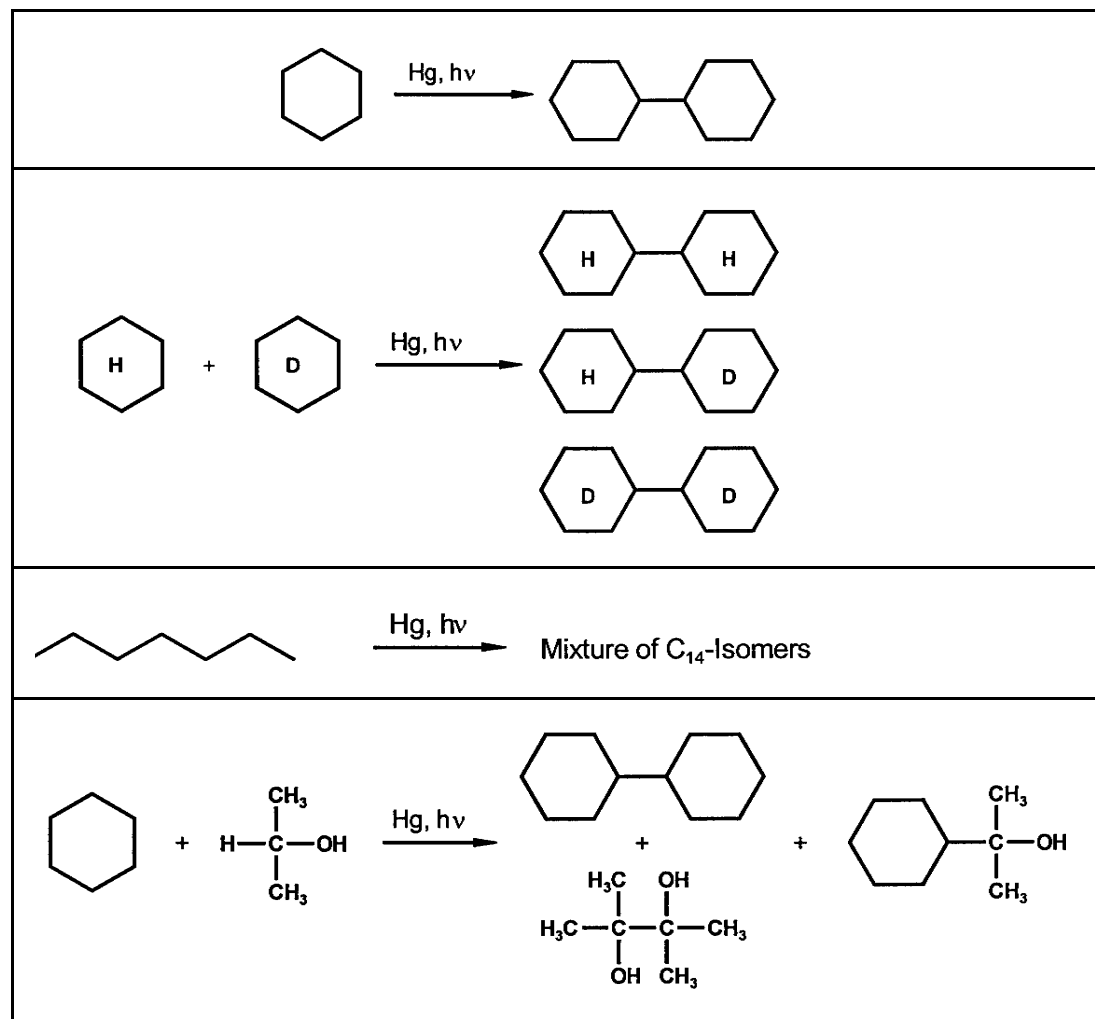
Figure 1. Oxidation of several substances with hydrogen peroxide / NOYORI-catalyst

The second example is that of microwave-promoted lipase-catalyzed reactions. The recent development of enzyme catalysis in organic synthesis for the kinetic resolution of racemates has attracted the attention of organic chemists because of their synthetic utility. The lipase-catalyzed transesterification has become a popular method in asymmetric synthesis. A major drawback of applying lipase-catalyzed reactions in organic synthesis is the low reaction rate. Immobilized *Candida antarctica* lipase (Novozym 435) catalyzed the reaction of some alcohols with ethyl acetate under multimode microwave irradiation and classical heating. We describe the results in dependence of time, temperature, and MW-power, cf. Figure 2.

Figure 2. Microwave-assisted esterification in presence of Novozym 435



The third example concerns first results of our new hyphenated MW-MWUV technique. In contrast to the "Microwave-Ultra Violet Combined Reactor" (Chemat (1999)) we combine the advantages of microwave heating with the properties of the MW-induced broad-band UV-spectra the same reactor system by use of electrodeless lamps.



Photochemistry has been shown to have a noticeable effect on many chemical reactions. This lab-system is quite suitable for organic synthesis and de-gradation.

We demonstrate its power with the help of dehydrodimerizations of selected hydrocarbons and their derivatives and by comparison with well-known papers of Crabtree ("Photochemical dimerization and functionalization of alkanes, ethers, primary alcohols and silanes"). Figure 3 informs exemplary.

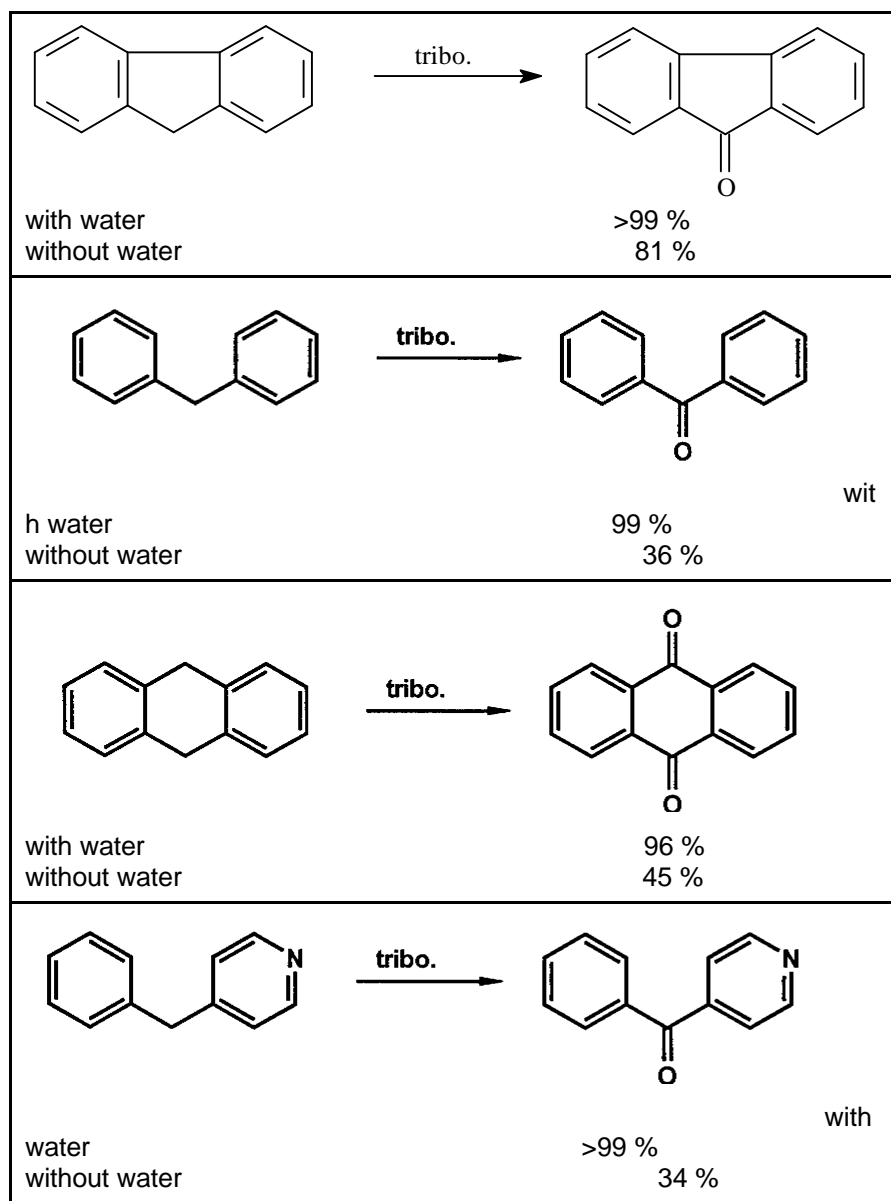
Figure 3. Examples of the dehydrodimerizations of selected hydrocarbons and their derivatives with MW-MWUV technique

The fourth example is concentrated on the tribochemical experiments. Numerous papers reported on very successful MW-assisted dry syntheses. Our interest was focused on the understanding of the overall procedure. Therefore we have repeated literature-known experiments and we have analyzed the prepared reaction mixture after the mechanical stirring and the MW-treatment, too. So we have found that in the case of oxidations with KMnO_4 the relatively high yields were already reached after the tribochemical act. Some preliminary results are given in Figure 4.

Summary

The four examples which have been presented illustrate the performance of microwave irradiation in chemistry. The diversity of possible microwave applications has been investigated, but the list is far from completeness.

Figure 4. Tribochemical conversion of benzyl-type hydrocarbons (planet ball mill "Pulverisette 7", Fa. Fritsch, 400 U/min, 10 min.)



WATER-BASED SYNTHESIS AND PURIFICATION OF MANNICH BASE MODIFIED POLYPHENOLS

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Abstract

New methods of producing and purifying Mannich base modified polyphenols and their copolymers without the use of organic solvents have been discovered and developed¹. The polyphenols, rather than being dissolved

initially in organic solvent, are dissolved in dilute alkaline solutions that ionize the required amount of phenol functionality to the phenoxide salt form. Formaldehyde solutions, which are typically inhibited with methanol, can be replaced by solid paraformaldehyde under these reaction conditions in order to avoid the use of any volatile organic solvent. The reaction proceeds further, faster and at lower temperatures than the solvent based method. After the Mannich formation is complete, an acid is typically added to react with the alkalizing agent and a portion of the newly acquired amine functionality. Viscosity and total solids can then be adjusted by dilution with water.

Passing this resulting solution through a common strong-acid type cation-exchange resin column in the H⁺ form quantitatively removes the sodium as well as any residual unreacted amine. Other small molecular weight cations are also removed including many Mannich reaction products of phenolic monomers. If separation of amine(s) or other small cations is not desired, a weak-acid type cation exchange resin may be employed. The crosslink density of the exchange resin types chosen and initial solution pH can also be varied to help tailor the specific removal or retention of small molecular weight ions.

Introduction

Many Mannich reaction products of polyphenols, selected secondary amines and formaldehyde are water soluble (or water soluble after acidification). Several have been found to produce unique and very useful surface active chelating polymers. These polymer solutions, and formulations containing them, have found several applications in the area of surface treatment. Early applications made use of poly(4-hydroxystyrene)-PHS/methylethanolamine/ formaldehyde derivatives. Dilute solutions slightly acidified with phosphoric acid are highly effective replacements for hexavalent chromium post-treatments over iron and zinc phosphate and other conversion coatings. These products are unique in their performance; greatly increasing salt spray resistance, paint adhesion etc., have the ability to be rinsed with fresh water after application (a reactive rinse) and are environmentally acceptable. Other processes that replace toxic heavy metal containing products were subsequently developed including: conversion coatings for many diverse metal substrates and dry-in-place/non-rinse formulations for coil coating applications. Effective low energy surface treatments and reactive rinse aids for plastic surfaces have also been formulated using these polymer types as components.

Although these Mannich derivatives have replaced toxic and environmentally unacceptable hexavalent chromium surface treatments to a great extent, and have general acceptance as a chromium replacement in the surface treatment industry, the products can contain up to 10% VOC before diluting to the proper operating concentration. Environmental rules on new manufacturing plants often take into account the total VOC use in a plant as a whole rather than just a particular operation. These newer rules tend to put these products under increasing scrutiny. The polymer itself is 99+% removable from wastewater by addition of small amounts lime followed by filtration. In fact, the presence of these polymers in the wastewater of manufacturing plants has been shown to significantly lower the amounts of trace heavy metal effluent released with treated wastewater. These chelating polymers strongly complex with many heavy metals resulting in increased precipitation and filtration efficiency. The solvent and free amine content are less easily treatable.

Several organic solvents can be used to solubilize the water insoluble phenolic polymer before the amine, water and liquid formaldehyde are charged. Once the Mannich base formation is complete, the reaction mixture is normally acidified and diluted with water. This can result in a product that may contain up to 10% volatile organic compounds. Mannich base containing products formulated without solvent increase shelf life, warm and cold temperature storage stability, reduce foaming during customer use in hard dilution water and can be supplied at a more appropriate pH values. However, removal of the organic solvent by distillation proved to be time consuming, expensive and difficult to carry to completion without undesirable condensation reactions.

Many Mannich derivatives of poly(4-hydroxystyrene) and formaldehyde utilizing the following solvent-free synthesis have been prepared using amines such as: N-methylethanolamine, N-methyl-D-glucamine, diethanolamine, ethylethanolamine, 2-methylaminomethyl 1,3-dioxolane and methylaminoacetylaldehyde dimethyl acetal. Many other amines and amino acids work as well. Many phenol containing polymers such as novolacs and tannins react similarly, using different levels of alkalizing agent.

Having good methods for final ion removal allows different approaches for the synthesis or modification of polyphenols. Many phenolic containing polymers dissolve in alkaline water by forming a phenoxide salt. Reactions of this solution with amine and paraformaldehyde typically react at lower temperatures and give higher yields in a shorter time period. The improved extent of reaction results in residual formaldehyde levels of

<100ppm rather than the typical ~800ppm for the PHS/methylethanolamine type solvent based manufacture. After reaction and acidification, the solvent-free solution is purified by passing it through a column of strong-acid type ion-exchange resin.

This deionization step very efficiently purifies the solutions by removing the alkalizing agent cation (such as sodium, potassium and/or quaternary ammonium), unreacted amine(s) and other small molecular weight cations in exchange for hydrogen ion (H^+).

The above purified polymer solutions can be further reacted with reagents, such as hydrogen peroxide to form the corresponding amine oxides, without concern that the peroxide may react with solvent, free amine or monomeric reaction products. Quaternary ammonium derivatives of these polymers have been prepared by reaction with methyl iodide, and the resulting iodide ions removed by anion-exchange. Many other syntheses, purification and reaction schemes worked well with other soluble polymers utilizing strong or weak anion-exchange and/or cation exchange resins. Some polymers in organic solvent solution or a mixed organic/water solvent also can be deionized. These examples demonstrate that these approaches are practical and have fairly universal application.

Many metal containing complexes of these polymers have been deionized without significant loss of chelated metal — this is important for the solvent-free synthesis of many of the newer conversion coating type formulations.

Evaluations were performed comparing the solvent-based Mannich derivatives to the new solvent-free technology using test methods such as: humidity, salt spray, cyclic corrosion, paint adhesion, formability, impact and other physical performance tests. Results demonstrated that the solvent-free systems showed equal to or better performance compared to the solvent-based products. It was concluded that the exchange resin chosen would retain its exchange capacity even after many dozen regeneration cycles. Full scale pilot plant production of 20,000 pound batches of the PHS/methylethanolamine based product were prepared after the installation of two 150 gallon ion-exchange columns in the production plant. The columns were filled with strongly acidic gel-type cationexchange resin beads. The columns were manually regenerated with 6% sulfuric acid solution and rinsed. After a key customer's new plant came under new VOC rules it was decided to move the major polyphenol based product to the solvent-free method of production. Newer counter-flow, fixed-bed style cation-exchange columns that were automated and much more efficient in their use of acid regenerate and rinse water were then designed and installed. Additional efficiency was realized after a "lead-lag" column setup was devised which required only one column be regenerated per cycle. The solution always passes through a freshly regenerated column last resulting in highly efficient deionization. The exchange resin has been regenerated over 100 times in the past year without the need for replacement.

Although the amounts and types of waste and/or inert product components resulting from the two types of synthesis make the solvent-free method much more environmentally sound, making this process truly "environmentally benign" would include making use of the resulting sodium bisulfate solution and rinse water produced during the cation exchange column regeneration. Recovering this waste and using it to formulate acid based cleaners and/or other products where sodium and sulfate content are not detrimental is under investigation. Free amine removed by the columns can be recycled by passing the caustic water for the next batch through the exchange resin and into the reactor. The column then contains only Na^+ and can then be regenerated with acid to return the exchange resin to the H^+ form. The amount of unreacted free amine can be significant for a bulky amine such as N-methyl-D-glucamine which only goes 80-90% to completion, but less so for amines such as N-methylethanolamine which will react 99+%.

It was a concern that the added production steps required for this type of process might increase the number of scrapped batches — but the opposite been the case. The increased complexity appears to be balanced by improved working conditions for production personnel: elimination of liquid formaldehyde, solvent vapors and many precautions related to fire hazard and personal exposure. The manual labor of pumping drums of solvent and formaldehyde into the reactor is eliminated. Fewer nitrogen tanks need to be replaced due to the greatly reduced need for inert blanketing and purges. Employee value and pride are also increased through the learning and use of new technical skills and the production of new environmentally superior products.

Simple parameters such as pH and conductivity are useful for automating the process —any problem with a column during deionization results in quickly rising values for both rather than a steady state. Simple solubility

and other tests are performed before the deionization step to ensure the columns will not be fouled by an incompletely reacted or incorrectly manufactured batch.

Summary

Several million pounds of the solvent-free product have been manufactured and sold in the past year. Hundreds of thousands of pounds of organic solvent release and their possible detrimental effects on the environment and ecosystem have been avoided. Raw material cost savings should pay for the added equipment quickly. Conversion of the remaining solvent-based polymer products to this process is very feasible. Manufacturing processes have been optimized for these newer formulations and product performance data in customer applications are now being evaluated. Most of the production procedures for these additional formulations have been put into place and are ready to utilize pending further performance testing results and customer approvals.

An initially limited working knowledge of ion-exchange technology led to these useful discoveries and applications. We are currently examining similar strategies for ecological and performance advantage in other polymeric systems and applications.

References

1. US5891952 (See also several related patents), McCormick, David, R., Lindert, Andreas, Pierce, John R., April 6, 1999, Henkel Corporation, Gulph Mills, PA.

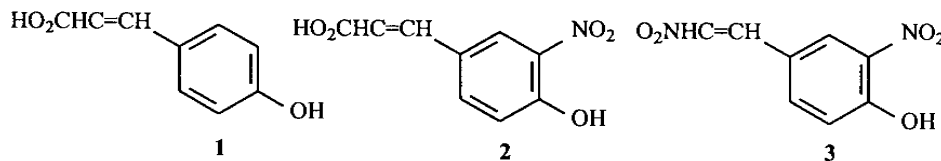
MICROWAVE ASSISTED ENVIRONMENTALLY BENIGN SYNTHESSES

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ABSTRACT

Using MORE (Microwave-assisted Organic Reaction Enhancement) Chemistry techniques, several organic reactions and processes have been developed that are environmentally benign. Reactions can be conducted easily, rapidly and efficiently in an unmodified domestic microwave oven in open vessels. High boiling polar solvents (or sometimes no solvents) are used as microwave energy transfer agents to give products in good yield and purity and with a high degree of "atom economy." For some products, stereoselectivity is observed. Reactions such as catalytic transfer hydrogenation and nitration of electron-rich aromatics can be conducted rapidly, safely, and efficiently using MORE chemistry. Nitration reactions have been conducted using HNO₃ diluted in water or HOAc to about 15% strength with greatly reduced reaction times and cleaner nitration products. Thus, the reaction of *p*-hydroxycinnamic acid **1** with dil. HNO₃ led in excellent yield in 2-3 min to dinitro compound **3** which is an unusual natural product.



INTRODUCTION

The pharmaceutical and fine chemical industries in America spend billions of dollars every year to control, treat, and dispose of hazardous waste. Reactions more benign to the environment have to be designed both for kilogram level operation and for production units. Green chemistry has to be practiced by not only major manufacturers but also small companies that are increasingly involved in "out-sourcing" by major pharmaceutical companies. Microwave assisted chemical synthesis is an emerging technology that can reduce pollution at the source and lead to high "atom economy." This technology can provide alternate pathways for manufacturing processes that would make the pharmaceutical industry more eco-friendly as well as more competitive.

Microwaves as Energy Source

Microwaves are a non-ionizing radiation that transfer energy to ions in solution and to other compounds with a

dipole. Glass, hydrocarbons and symmetrical molecules absorb very little microwave energy. Solvents such as water, *N,N'*-dimethylformamide (DMF), chlorobenzene, anisole and compounds with dipole moment (e.g., esters, amides, and alcohols) absorb microwave energy efficiently. Microwaves have the ability to penetrate to a considerable depth (several cm) depending on the frequency of the radiation and the nature of the material in terms of dipole moment and "loss factor". Energy is provided to the appropriate molecules directly without heating the glass container. Radiant energy, however, heats the surface only. Thus, reactions that require several hours under conventional heating are completed in a matter of minutes under microwave irradiation. For example, the Diels-Alder addition of maleic anhydride to anthracene was conducted in our laboratory in diglyme (bp 162°C) in 90% yield in a microwave oven; the time of reaction was one minute whereas the conventional synthesis in refluxing benzene (bp 80°C) requires 90 minutes.

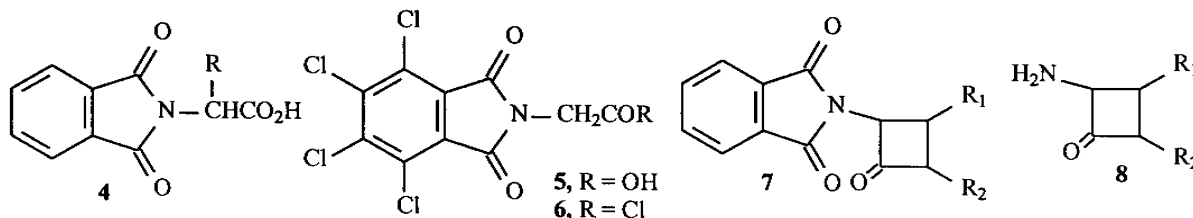
Microwave-induced Organic Reaction Enhancement (MORE) Chemistry

Two seminal papers appeared in 1986 which reported that a variety of organic reactions could be completed in sealed systems in domestic microwave ovens in a matter of minutes; a few explosions due to a rapid rise of temperature and pressure were also reported. To avoid explosions, some laboratories designed "dry" or solventless reactions conducted with the reactants deposited on clay, silica gel, alumina or other solid supports. Obviously, such reactions cannot be suitable for large-scale synthesis in a flow system.

We have taken a different approach and developed non-traditional methods for using microwave irradiation for conducting a wide variety of organic reactions that are fast, safe, inexpensive, and friendly to the environment. Our techniques involve reactions in open glass vessels using minimal quantities of high boiling polar solvents (or no solvents if one of the reactants is a liquid). The reaction mixture is maintained at a temperature at least 20°C below the boiling point of the solvent: reflux condensers are thus unnecessary. For condensation reactions where water (or some other small molecules) is a reaction product, a reaction temperature of 120-130°C seems to be near optimum. We have found it convenient and economical to use a minimal amount of solvents because in most cases, a room temperature slurry provides adequate solubility for reactants during the rapid rise in temperature that occurs under microwave irradiation. Less solvent used means less solvent waste and, therefore, reduced pollution. A few illustrative examples of MORE chemistry techniques for organic synthesis are provided below.

N-Phthaloyl amino acids and peptides

In 1973 we reported that the reaction of phthalic anhydride with α -amino acids to form their phthaloyl derivatives (**4**) can be conducted in refluxing toluene using triethylamine as a catalyst. A Dean-Stark water separator was employed for removing the water formed in the reaction. For phthaloylation on a tenth-molar scale of amino acids, the reaction time was several hours. Under microwave irradiation this type of reaction is complete in a few minutes if DMF is used as the reaction medium in place of toluene which does not absorb microwave energy efficiently. No water separator is needed, nor is stirring of the reaction mixture necessary because microwave energy is absorbed directly by the reactants. Reactions have been conducted on 200-300 g scale in 10-15 min. Di- and tri-peptides were also derivatized rapidly by this method. Recently, we have substituted tetrachlorophthalic anhydride for phthalic anhydride and prepared *N*-tetrachlorophthaloylglycine (**5**) on a molar scale in 90% yield. Microwave irradiation was required for about 8 min.



Reaction of tetrachlorophthalimido acetylchloride (**6**) with Schiff bases in methylene chloride solution in presence of triethylamine gave a mixture of *cis*- and *trans*- β -lactams. The corresponding MORE chemistry version (with chlorobenzene in place of methylene chloride) led to almost pure *trans*- β -lactam (**7**) in high yield when the bulk reaction temperature was about 100°C. Interestingly, the imine from cinnamaldehyde and *p*-anisidine gave only the *cis*- β -lactam at all levels of microwave irradiation. Removal of the tetrachlorophthaloyl protective group was effected by reaction with ethylenediamine under microwave irradiation for a few minutes. The α -amino- β -lactams (**8**) prepared in this manner are useful synthons for various types of biologically active compounds.

Catalytic Transfer Hydrogenation

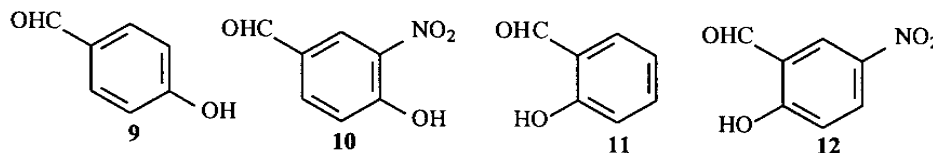
A valuable MORE Chemistry technique of wide applicability is catalytic transfer hydrogenation using ammonium formate as the hydrogen source. We have conducted reduction and hydrogenolysis reactions by this method in just a few minutes and in nearly quantitative yield. Ethylene glycol or 1,3-propanediol (bp about 200°C) is a convenient medium for reaction at about 130°C. Thus, the hydrazone of benzophenone was prepared by reaction with hydrazine in ethylene glycol under microwave irradiation. Hydrogenolysis of this derivative with ammonium formate under microwave irradiation in the presence of 10% Pd/C catalyst led to diphenylmethylamine in high yield. In a similar fashion a phenyl pyruvate ester was converted to the corresponding phenylglycine ester via a phenylhydrazone prepared in a microwave assisted reaction.

Microwave-assisted Aromatic Nitration

At Stevens several approaches to eco-friendly nitration have been developed that eliminates the need for strong acids. Industrial or laboratory use of conc. HNO_3 and H_2SO_4 is hazardous to health because of the emission of nitrogen oxides and the problem of the disposal of residual strong acids which are hazardous to the environment. Preliminary work at Stevens shows that a very eco-friendly nitration technique is to use a mixture of sodium nitrate and acetic acid under microwave irradiation; mono-nitrates of phenolic compounds are formed in a few minutes and in high yield. A variant of this method is to use acetic acid with dil. HNO_3 , under microwave irradiation — either as a batch process or in a flow system.

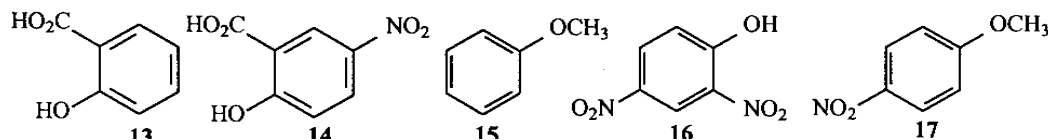
Laszlo has reported that the nitration of certain aromatic compounds can be achieved upon reaction for several hours with $\text{Cu}(\text{NO}_3)_2$, or $\text{Fe}(\text{NO}_3)_3$ deposited on Montmorillonite clay, acetic anhydride and a chlorinated solvent. Data from our laboratory have demonstrated that "Clayzinc" [$\text{Zn}(\text{NO}_3)_2$ deposited on clay] can be used for mononitration of phenol ethers in a few minutes under microwave irradiation in an unmodified domestic microwave oven. Zinc salts are more eco-friendly than copper salts. Additionally, microwave irradiated rapid nitration with Clayzinc can be conducted without the use of acetic anhydride or chlorinated solvents — thus improving the "atom economy". A few specific examples of these nitration reactions are provided here.

When finely powdered 4-hydroxybenzaldehyde (**9**) was added to aqueous nitric acid (about 15% HNO_3) and the suspension was irradiated in a domestic microwave oven, the starting material disappeared in 1-2 minutes; in the next 1-2 minutes yellow crystals appeared. The nitration was complete in less than 5 minutes and nearly pure 4-hydroxy-3-nitrobenzaldehyde (**10**) was obtained in 70% yield by simple filtration and washing with water. This reaction was also conducted successfully on a 50-g scale. The bulk temperature of the reaction mixture was about 80°C. A similar reaction with salicylaldehyde (**11**) led to pure 2-hydroxy-5-nitrobenzaldehyde (**12**) in 64% yield after 90s of irradiation.



Nitration under Monomodal Microwave Irradiation

For obtaining a close control on the input of microwave energy into nitration reactions, we conducted experiments in a Prolabo Synthwave S402 apparatus monitored by a computer. The microwave energy required to raise the temperature of a volume of water to 90°C was reduced by 80% when a drop of HNO_3 was added to the water showing thereby that the ions from the acid were very efficient in absorbing microwave energy. The nitration of salicylic acid (**13**) with dilute HNO_3 was then conducted using 15-20 watts of power. A single product was obtained which was identified as 5-nitrosalicylic acid (**14**). At higher power levels in a domestic microwave oven, a mixture of products was obtained.



Irradiation at high power for 2 min 20 s of anisole (**15**) and aq. HNO_3 gave about 40% yield of 2,4-dinitrophenol (**16**) with only a trace amount of 4-nitroanisole (**17**).

It is remarkable that demethylation was achieved by dil. HNO_3 in such a short time. Using the Prolabo Synthwave S402 it was found that much lower levels of energy can provide mostly 4-nitroanisole (**17**).

Efficient Synthesis of a Marine Natural Product

In the course of a collaborative Indo-US research project an unusual dinitro compound (**3**) had been isolated. Biosynthetically, (**3**) is related to 4-hydroxycinnamic acid (**1**). When **1** was subjected to the action of dil. aq. HNO_3 under microwave irradiation, **3** was obtained in 60-70% yield. In some experiments it was possible to isolate 4-hydroxy-3-nitro-cinnamic acid (**2**) as an intermediate. It is remarkable that the carboxy group was replaced so easily by a nitro group. A highly efficient and a very rapid microwave assisted conversion of **1** to **3** can be achieved by reaction with 15% HNO_3 in HOAc. Thus 1 g of **1** was transformed in 92% yield to **3** in 15 sec of irradiation in a domestic microwave oven (600-800 watts).

SUMMARY

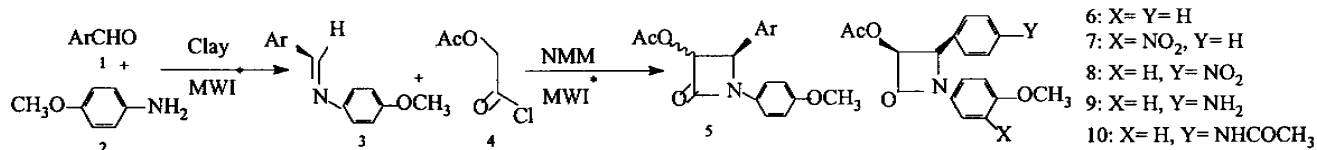
Most of the conventional nitration methods are ecologically unfriendly as they involve such reagents as concentrated sulfuric acid, phosphoric acid, trifluoroacetic anhydride, etc. The microwave assisted nitration reactions reported here are much friendlier to the environment than their conventional counterparts.

MICROWAVE ASSISTED ECO-FRIENDLY SYNTHESIS OF INTERMEDIATES FOR TAXOL™ AND ANALOGS

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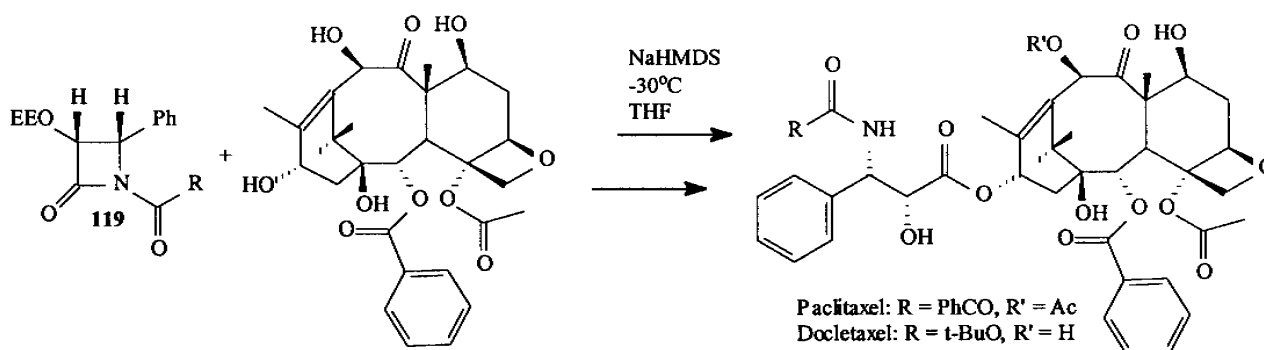
ABSTRACT

The antitumor drug Taxol™ and analogs are of great current interest. Advanced intermediates (e.g., **6**, **8**, **9**, **10**) for their semi-synthesis have been prepared conveniently and rapidly in open vessels by microwave-assisted, multi-step reactions. Starting with an aldehyde **1**, and the amine **2**, the Schiff base **3**, was prepared in 2-3 min in a domestic microwave oven in a solventless reaction catalyzed by Montmorillonite clay. The acid chloride **4**, a base (NMM), and a limited amount of a solvent were added to **3**, and *cis* or *trans* β -lactam **5** was obtained after microwave irradiation (MWI*). Nitration of **6** to **7** was effected in minutes by microwave assisted reactions with "Clayzinc". Reduction of **8** with indium in water gave the amine **9** which could be variously transformed (e.g., to **10**) to provide easy access to novel analogs of Taxol™.



INTRODUCTION

The antitumor drug Taxol™ and its analog Taxotere are now in wide clinical use. Both of these drugs are now available through semisynthesis using an appropriate β -lactam (for example, **5**) as the intermediate. Analogs of these drugs are also under study in many laboratories.



In recent years we have shown that diversely substituted β -lactams can be prepared efficiently and rapidly under microwave irradiation. The Microwave-induced Organic Reaction Enhancement (MORE) chemistry techniques that we have devised allow reactions to be conducted in open glass vessels. We have found that the use of high boiling polar liquids as the reaction medium simplifies the reaction set up. Much of our work has been conducted in commercial domestic microwave ovens.

For a more detailed study we have used the Prolabo Synthwave 402 apparatus which allows computer control of the energy input and monitors the reaction temperature. In the interest of devising an ecofriendly synthesis of β -lactam intermediates for Taxol and analogs, we have studied microwave assisted reactions as alternatives to the conventional approaches.

Microwave Assisted Synthesis

The first step in our synthesis was the formation of the schiff base **3** from an aromatic aldehyde **1** and *p*-anisidine **3**. Following the method of Varma et al., commercially available Montmorillonite clay was used as a catalyst and a solventless reaction was conducted successfully under microwave irradiation in a domestic microwave oven. Only 2-3 min were required for the completion of the reaction as shown by TLC monitoring. It is possible that the clay adsorbs the water formed in this reversible reaction and thus displaces the equilibrium.

Stereocontrol of β -Lactam Formation

The conventional method for the next step involves the reaction of the Schiff base **3** with acetoxyacetyl chloride **4** in presence of triethylamine in methylene chloride solution at room temperature for a period of a few hours. For carrying out the reaction in a domestic microwave oven, the low boiling base triethylamine was replaced with *N*-methylmorpholine (bp 116°C); also methylene chloride was replaced by the higher boiling, polar solvent chlorobenzene (bp 132°C). At lower power settings of the microwave oven, a mixture of *cis* and *trans* β -lactam **5** was obtained. At higher power settings with the bulk temperature of the reaction mixture around 120°C , the *trans* β -lactam was 95% of the mixture.

It was observed that under these reaction conditions the *cis* β -lactam did not isomerize to the *trans* β -lactam. It would appear that the *cis* and the *trans* isomers are formed by two different pathways and that the pathway to the *trans* isomer is favored by a higher temperature of the reaction. Thus, the conventional, low temperature condition can be used for preparing the *cis* compound while the microwave assisted reaction can be employed for obtaining the *trans* compound.

One Pot Reaction for β -Lactam Synthesis

We have been able to combine the two reaction steps in a one pot reaction for preparing β -lactams in good yield. It is unnecessary to remove clay from the Schiff base formed in the first step. Also, it is possible to replace the chlorinated solvent in part by the more eco-friendly solvent anisole for reactions under microwave irradiation.

Nitration of β -Lactams

Nitration of the *p*-methoxyphenyl group in **6** to give **7** was achieved in good yield by microwave assisted reaction using zinc nitrate deposited on Montmorillonite clay (Clayzinc) as the nitrating agent. This nitration without nitric acid is environmentally more benign than several other conventional nitrating methods.

The β -lactam **7** was prepared by using *p*-nitrobenzaldehyde as the aromatic aldehyde **1**. The nitro group in **8** was easily reduced to the amino group (as in **9**) and acylated to give an amide (as in **10**). These β -lactams are

convenient intermediates for a variety of analogs of Taxol.

SUMMARY

Reactions under microwave irradiation for a few minutes have been developed for eco-friendly synthetic approaches - with limited amounts of solvents or no solvents to β -lactam intermediates for Taxol and analogs.

NEW PROTOCOLS FOR THE UTILIZATION OF ETHYLENE AND PROPYLENE IN FINE CHEMICAL SYNTHESIS

T. V. (Babu) RajanBabu

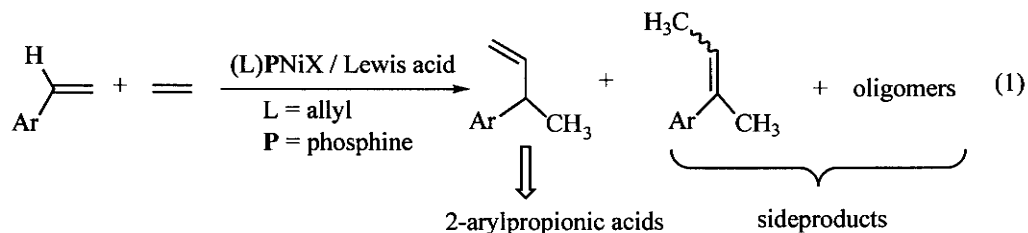
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ABSTRACT

In this era of heightened environmental awareness and the ever-increasing demand for higher efficiency from chemical processes, one of the major challenges facing organic synthesis is the selective incorporation of abundantly available carbon, hydrogen, oxygen and nitrogen sources into other common substrates. In this context, we have discovered new protocols for highly selective and nearly quantitative codimerization of ethylene or propylene and various unfunctionalized vinylarenes. Under these conditions, which are compatible with a wide variety of functional groups, hydrovinylation of strained olefins can also be accomplished. Also presented are possible strategies for stereochemical control, including a crucial role for hemilabile ligands in enantioselective catalysis. Potential applications of this chemistry include the synthesis of widely used antiinflammatory agents such as ibuprofen and naproxen.

INTRODUCTION

The astonishingly high turnover frequency ($625,000 [\text{propylene}][\text{Ni}]^{-1} [\text{h}]^{-1}$) observed for $[\eta^3\text{-(allyl)Ni(PR}^3\text{)}]^+ [\text{RAIX}_3]^-$ in the catalytic dimerization of propene to a mixture of C_6 olefins makes this system among the most active homogeneous catalysts for carbon-carbon bond-forming reactions.¹ Applications of this chemistry in fine chemical synthesis would be especially attractive if the reaction can be extended to hetero-dimerizations and sufficient selectivity can be achieved. Among these reactions, codimerization of ethylene and vinylarenes (hydrovinylation) has attracted the most attention because the product 3-aryl-1-butenes are potential intermediates for widely used 2-arylpropionic acids such as ibuprofen, naproxen and ketoprofen (eq 1). Even though the hydrovinylation reaction has a long history, careful examination of published work² reveals that except for an isolated case reported by Wilke³ no other catalyst gives satisfactory yield and selectivity in this potentially important reaction. High pressures of ethylene and metal components incompatible with sensitive organic groups often limit the utility of many of the reported procedures.

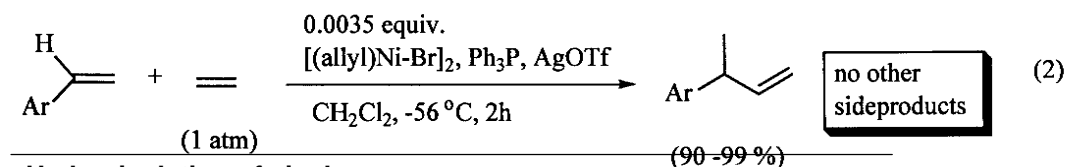


RESULTS AND DISCUSSION

A New Protocol for Hydrovinylation of Vinylarenes

Considering the details of the mechanism of the reaction, we reasoned that the scope and selectivity of the hydrovinylation could be significantly improved by changes in the phosphine and of the counter anion.⁴ After an extensive scouting program in which we systematically varied the phosphine and the counter ion, a new protocol was arrived at. We find that the hydrovinylation of various vinylarenes proceeds with *unprecedented* chemical yield and selectivity when a combination of allylnickel bromide dimer, a weakly coordinating counter ion (e.g., OTf) and a tertiary monophosphine is employed as the precatalyst (eq 2 and Table 1). Typically the reaction is carried out at -56°C in methylene chloride as the solvent under 1 atmosphere of ethylene pressure using 0.007 equiv. of the catalyst. Under these conditions no oligomerization of either the vinylarene or ethylene is detected. In sharp contrast to the previously reported Lewis acid-mediated reactions, vinylarenes with Lewis basic centers

such as oxygen, chlorine and bromine undergo the reaction with remarkable ease (entries 3, 5 and 7). 2-Methoxy-6-vinylnaphthalene, 4-isobutylstyrene and 3-fluoro-4-phenylstyrene (entries 5, 6, 7), all potential precursors for important antiinflammatory agents, gave excellent yields of the expected hydrovinylation products. Hydrovinylation product of 4-bromostyrene (entry 3) is another potentially important precursor that could be transformed into a variety of useful intermediates via organometallic cross-coupling reactions.



Hydrovinylation of vinylarenes

Entry	Substrate	% Yield ^a	Conditions ^b
1.	styrene	>95 (99 ⁺)	(i)
2	4-methoxystyrene	>95 (98)	(i)
3	4-bromostyrene	>95 (98)	(i)
4	2-vinylnaphthalene	(99 ⁺)	(i)
5	6-MeO-2-vinyl-naphthalene (MVN)	(90) (97)	(i), 0.5 mol% cat. (ii)
6	4- <i>i</i> -Bu-styrene	>90 (99 ⁺) >97 (99 ⁺)	(i), 1.4 mol% cat. (ii)
7	3-F-4-Ph- styrene	(80)	(i)

^aIn brackets are the yields estimated by gas chromatography.

^b(i) [(allyl)NiBr]₂, (0.35 mol%)/Ph₃P/AgOTf/CH₂Cl₂/-55 °C/2 h

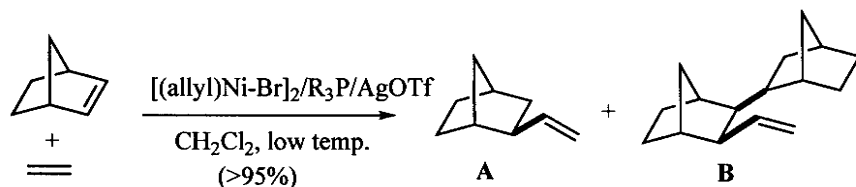
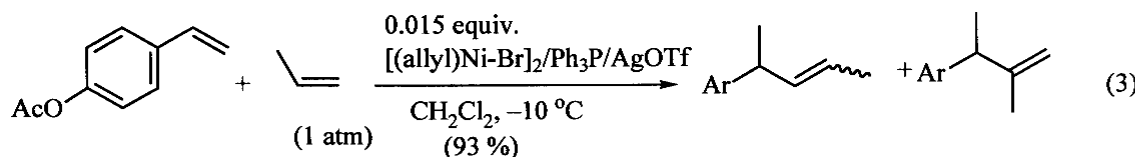
(ii) [(allyl)NiBr]₂, (0.70 mol%)/(*R*)-MOP /Ar₄B⁺Na/CH₂Cl₂/-56 °C/2h.

Other

Heterodimerization Reactions

Unlike heterodimerization reactions of ethylene, no synthetically useful heterodimerization reaction using propene is known. We find that propene reacts with styrene and substituted styrenes under conditions slightly modified from what was previously described for ethylene (eq 3) giving excellent yields of the expected products. An example of a substrate with a Lewis basic acetoxy group is shown in eq 3. The reaction with propene proceeds at higher temperature (-15° to 10 °C vs -56 °C for ethylene), especially in the case of

the more electron-deficient styrene derivatives. As expected, a mixture of regioisomeric products (with propene-C₁ addition to the benzylic position as the major one) is obtained.



We find that the protocol using [(allyl)NiBr]₂/phosphine/AgOTf works equally well for the hydrovinylation of norbornene, the course of the reaction being dependent on the phosphine

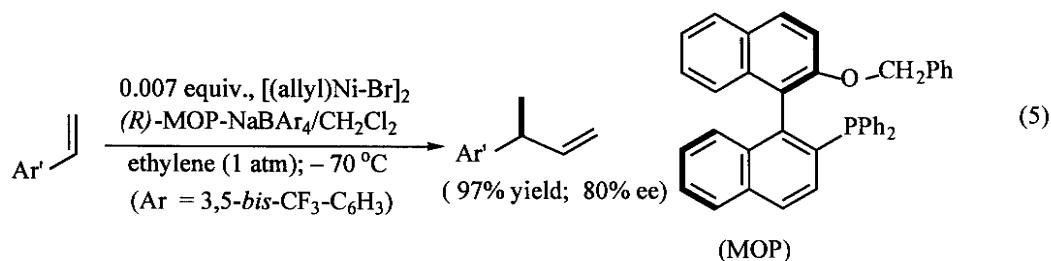
that is employed. Tricyclohexylphosphine gives the expected 1:1 adduct, whereas triphenylphosphine gives a 2:1 adduct between norbornene and ethylene (eq 4).

Phosphine	Cone angle	Temp.	A	B
[cyhex] ₃ P	180°	-70 °C	100	0
Ph ₃ P	145°	-55 °C	1	97

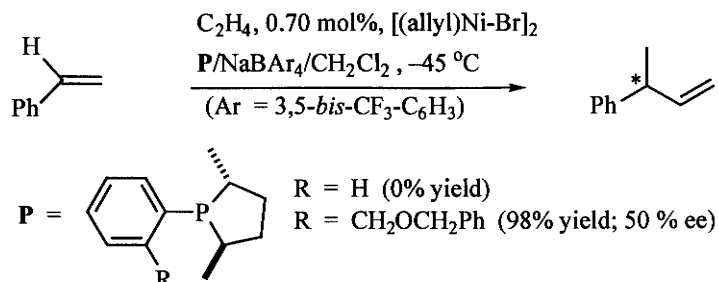
Asymmetric Hydrovinylation Reactions

In our initial attempts to find a broadly applicable asymmetric version of this reaction we considered the requirement of a coordination site for ethylene on the putative cationic Ni intermediates, and chose 2-diphenylphosphino-2'-methoxy-1,1'-binaphthyl (MOP) ligand⁶ which carries, in addition to the tertiary phosphine, a methoxy group, which could now serve as 'hemilabile' ligand (eq 5).⁷ The new protocol which uses the tetrakis-[3,5-bis(trifluoromethyl)phenyl]borate (TFPB) anion⁸ gave a substantially improved catalyst vis-à-vis the corresponding triflate derivative. 2-Methoxy-6-vinylnaphthalene (MVN) and 4-isobutylstyrene gave nearly

quantitative yields (> 99 %) of the products in 80 % and 40 % ee (S-isomers) respectively (eq 5).⁴ A number of control experiments have confirmed the crucial role of the 'hemilabile' of the

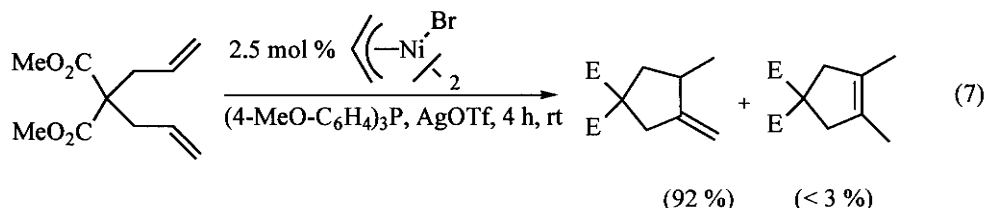


alkoxy group in the reaction.



Since the original discovery of the importance of a hemilabile atom in a ligand for high enantioselectivity, we have recognized that this effects is equally important in a number of other monophosphines that promote the hydrovinylation and other related reactions. In addition,

we have found that a synergistic effect of hemilabile groups and counterions could be employed in the design of highly efficient catalysts for C-C coupling reactions. An example of a 1,5-dialkylphospholane is shown in eq 6.



We are also pursuing other applications of related reactions for the synthesis of carbocyclic and heterocyclic compounds (eq 7).⁹

SUMMARY

The heterodimerization of olefins appears to have great potential as a carbon-carbon bond forming reaction when the two olefins involved have different reactivities. With ethylene as one of the reactants, this difference could have its origin in electronic (e.g., vinylarenes, dienes) or strain (e.g., bicyclo[2.2.1]heptenes) factors. The reactions are highly catalytic, and the conditions, tolerant to a wide spectrum of common organic functional groups. With the discovery of a number of widely different 'tunable' ligands, and of the new control elements (e.g., hemilabile ligands and counterion effects), the prospects of developing *practical* enantioselective versions of these reactions appear imminent.

ACKNOWLEDGEMENTS

This work was done in collaboration with the following postdocs and graduate students: J. Jin, M. Nandi, N. Nomura, H. Park, and B. Radetich. Financial assistance by the NSF (CHE-9706766), EPA (R826120-01-0), and the PRF(ACS) is gratefully acknowledged.

REFERENCES

- Y. Chauvin, H. Olivier in *Applied Homogeneous Catalysis with Organometallic Compounds Vol. 1* (Eds.: B. Cornils, W.A. Herrmann), VCH, New York, 1996, p. 258.
- For two recent reports, see: (a) Muller, G.; Ordinas, J.I. *J. Mol. Catal. A: Chem.* **1997**, 125, 97.; (b) R. Bayersdörfer, B. Ganter, U. Englert, W. Keim, D. Vogt, *J. Organomet. Chem.* **1998**, 552, 187.
- G. Wilke, J. Monkiewicz, H. Kuhn (Studiengesellschaft Kohle), US Patent 4 912 274, 1990. *Chemical Abstracts* **1991**, 114, 43172.
- N. Nomura, J. Jin, H. Park, T.V. RajanBabu, *J. Am. Chem. Soc.* **1998**, 120, 459.
- See references 2(b) and (3) for other asymmetric hydrovinylation reactions.
- Y. Uozumi, A. Tanahashi, S.-Y. Lee, T. Hayashi, *J. Org. Chem.* **1993**, 58, 1945.

7. Britovsek, G.J.P.; Keim, W.; Mecking, S.; Sainz, D.; Wagner, T. *J. Chem. Soc., Chem. Commun.* **1993**, 1632 and references cited therein.
 8. For a recent application of TFPB salts, see: G.M. DiRenzo, P.S. White, M. Brookhart, *J. Am. Chem. Soc.* **1996**, *118*, 6225.
 9. Radetich, B.; RajanBabu, T.V. *J. Am. Chem. Soc.* **1998**, *120*, 8007.
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ALKENE HYDRATION AND AMINATION

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ABSTRACT

Calculations have been carried out on the hydration and amination of alkenes to give alcohols and amines respectively. This density functional theory computational study shows both reactions to be exothermic. The enthalpies are in the -7 to -6 kcal mol⁻¹ range for acyclic alkenes. Computationally, unsubstituted alkenes, or those substituted with electron donor groups, undergo hydration and amination reactions more readily than electron deficient alkenes, and branched isomers are favored over linear ones. Strained bicyclic dienes have enthalpies that range between -11 to -33 kcal mol⁻¹. For aqueous systems, ruthenium(II) and palladium(0) TPPTS complexes have been used for the hydration of 1-octene to 1-octanol, and for biphasic systems, calix[4]arenes having both ligating and methoxy poly(ethylene glycol) groups appended to their rims have been synthesized, and found to be mostly soluble in both water and aqueous poly(ethylene glycol).

INTRODUCTION

The direct hydration or amination of alkenes with water or ammonia is a potential route for the synthesis of alcohols and amines respectively. A challenge in developing homogeneous catalysts for such reactions is that they must usually be carried out in a two-phase systems. The majority of homogeneous catalysts are soluble in the organic phase, but increasingly there is an interest in using ones that partition into the aqueous component. In these cases, a single phase catalyst system will be realized only if the alkene is water soluble.

RESULTS AND DISCUSSION

The results of our computational studies are collected in the Table. Although the absolute values of these 298K energies are subject to variations resulting from the computational model, for the consistent model we have used across the series, the relative data are reliable. As a test of the reliability of our data we have carried out several of the calculations at the MP2 6-311G* level. The absolute enthalpies of the compounds are in each case approximately 0.25% higher in energy than those obtained by our Beeke-Percew method, but the calculated reaction enthalpies are unchanged.

These computational data show that each reaction is exothermic, and that the exothermicities of both the hydration and amination reactions are closely similar. The formation of branched isomers is favored over linear ones, which correlates with the known favorability of an alkene to undergo Markovnikov addition. Also, carboxylic acid substituents on the alkene result in a less negative enthalpy change than is observed for a more electron rich alkene. By contrast, the analogous alkenes with hydroxymethyl substituents preferentially undergo addition at the substituted alkene. The addition of water or ammonia to an alkene is more exothermic for a strained bicyclic diene than for an unstrained linear alkene. The effect of strain energy is also reflected in the observation that the addition of a second molecule of water or ammonia to a diene results in a less negative enthalpic change than would be observed if the addition were to be occurring at the first alkene bond of the diene.

We have also begun to ascertain whether water soluble tertiary phosphine complexes are catalytically active for the hydration or amination of the terminal alkenes 1-octene and 1-dodecene. Although reproducibility is problematic, we have observed that preparations of TPPTS complexes of ruthenium(II) and palladium(0) can

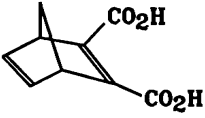
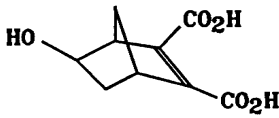
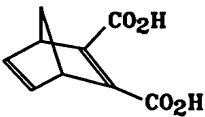
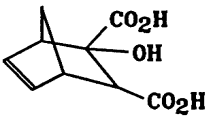
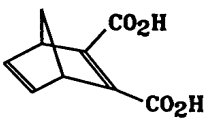
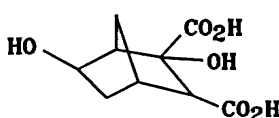
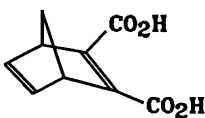
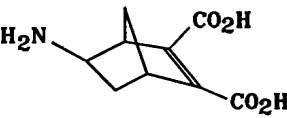
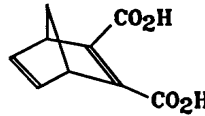
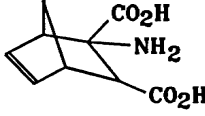
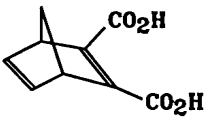
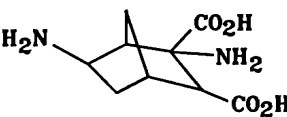
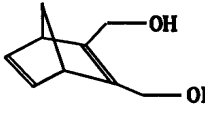
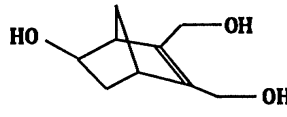
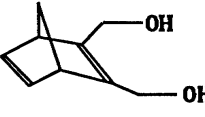
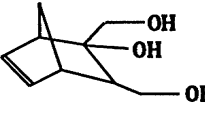
give up to 7% conversion of 1-octene into 1-octanol, which represents a catalytic turnover number of 6 based on the metal complex. The mass spectrum of the octanol product closely matches that of 1-octanol, rather than 2-octanol, 2-octanone, or the aldehyde octanal. The failure to observe aldehyde or ketone argues against nucleophilic attack of water at a coordinated 1-octene. Since a terminal alcohol would result from a reductive elimination from a hydroxyalkyl intermediate, it is plausible that the initial step involves an addition of water to a low valent complex.

Calix[4]arenes with both ligating and methoxy poly(ethylene glycol) groups appended have been synthesized using several approaches. These involve the formation of sulfonyl ester groups on the wide rim, Schiff base derivatives on the narrow rim, and thioether groups on both the wide and narrow rims. These compounds are mostly soluble in both water and aqueous poly(ethylene glycol), and are planned as precursors for biphasic catalytic systems.

Table. Calculated Enthalpies of Reaction (in kcal/mol)

Alkene	Addend	Product	Reaction Enthalpy
	+ H ₂ O		-7
	+ NH ₃		-7
	+ H ₂ O		-13
	+ NH ₃		-8
	+ H ₂ O		-14
	+ H ₂ O		-10
	+ NH ₃		-16
	+ NH ₃		-11
	+ H ₂ O		-11
	+ H ₂ O		-12
	+ NH ₃		-10
	+ NH ₃		-12

Table. Calculated Enthalpies of Reaction (in kcal/mol) (continued)

Alkene	Addend	Product	Reaction Enthalpy
	+ H ₂ O		-21
	+ H ₂ O		-11
	+ 2 H ₂ O		-25
	+ NH ₃		-20
	+ NH ₃		-14
	+ 2 NH ₃		-29
	+ H ₂ O		-20
	+ H ₂ O		-33

ACKNOWLEDGMENTS

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REFERENCE

H. Fred Koch, Luc A. Girard, D. Max Roundhill, *Polyhedron*, in press.

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Moving Toward Industrial Ecology

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**GREENER
SOLVENTS**

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USING STRUCTURE-PROPERTY RELATIONSHIPS TO DESIGN "GREENER" SOLVENTS

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Solvents constitute a major source of pollution for the chemical and pharmaceutical industries. Substituting hazardous solvents with ones more environmentally compatible is a viable means of pollution prevention. However, choosing the right solvent is a difficult process often done in an ad hoc manner. We will present a systematic approach to selecting solvents using structure-property relationships. Structure-property relationships are used to quickly and efficiently screen candidate solvents, ensuring they have acceptable properties including adequate solvency, low flammability, and low toxicity. Using structure-property relationships also enables us to examine the tradeoffs that may need to be made between solvent performance objectives. Examples will be presented for selecting solvents for liquid extraction and crystallization. We will also discuss how the same methodology can be used to design other "green" chemical products in addition to solvents.

ROOM TEMPERATURE IONIC LIQUIDS AS ALTERNATIVES TO ORGANIC SOLVENTS IN LIQUID/LIQUID EXTRACTION

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Room Temperature Ionic Liquids (RTIL) are emerging as novel replacements for Volatile Organic Compounds (VOCs) traditionally used as industrial solvents. RTIL are liquids that are composed entirely of ions and in this sense resemble the ionic melts which may be produced by heating normal metallic salts such as sodium chloride to high temperature. RTIL are currently being investigated as alternate reaction media, allowing controlled production of desired products with a minimum of waste.

The Montreal Protocol¹ identified the need to reevaluate chemical processes to take account of their environmental impact especially with regard to the use of VOC solvents. Yet, while the new paradigm in industrial ecology stresses the role of clean manufacturing processes in providing the basis for sustainable technologies, worldwide usage of VOCs in excess of 5 billion dollars² indicates the large quantity consumed per annum, even with new international treaties which are severely limiting the amount which can be released in plant effluents. The abbreviation VOC has become synonymous with a plethora of social, economic, and ecological hazards, and such use seems increasingly anachronistic. It is thus incumbent upon the research community to explore the inherent benefits of alternative technologies to replace VOCs and reduce the associated health risks, volatility, environmental, and human health and safety concerns that accompany exposure to organic solvents.

Room temperature ionic liquids offer a highly solvating, yet non-coordinating medium in which a number of organic and inorganic solutes may be dissolved.³ They are non-volatile, non-flammable, have high thermal stability,³ and are relatively undemanding and inexpensive to manufacture. Many RTIL are liquids over a wide temperature range (for some this range may exceed 300 °C) and RTIL with melting points as low as -96 °C are known.³ The constituents of RTIL (being ionic) are constrained by high coulombic forces and thus, exert practically no vapor pressure above the liquid surface. These features, and the potential to reduce pollution in industrial processes, have led to current investigations of RTIL as alternative reaction media for a variety of applications that use organic solvents. Some of the current research areas include the following:

- **Catalysis:** RTIL can act as both catalyst and solvent.⁴
- **Synthesis:** RTIL have unique solvent effects which limit conventional solvation and solvolysis, may enhance reaction rates and selectivity, and reduce side reactions.⁵
- **Electrochemistry:** RTIL can have large electrochemical windows, have high conductivities, and may limit solvolysis.⁶
- **Separations:** RTIL are known which are moisture stable, water immiscible, and have high capacity for organic solutes (up to 50% v/v% solutions of benzene have been reported). A wide variety of aryl organic molecules partition favorably to the ionic liquid phase from water and early results lead to the expectation that applications may be selected in the first instance based on hydrophobicity data (e.g., 1-octanol/water partitioning coefficients).⁷

The majority of RTIL studies reported in the literature to date have utilized large, asymmetric organic cations. The most common examples include *N*-alkylpyridinium and 1-alkyl-3-methylimidazolium (Rmim, Fig. 1) cations in which the alkyl group may be varied to fine-tune the physical properties of the RTIL. For example, notable changes in melting point are observed as the length of the alkyl chain increases in [Rmim][PF₆] ionic liquids; the ethyl derivative ([emim][PF₆]) melts at 62 °C⁸ while at room temperature, the butyl (mp = 4 °C), hexyl (mp = -78 °C), and octyl (mp = -72 °C) are liquids.⁹ When R is increased to the decyl group ([dmim][PF₆]), the salt is a solid at room temperature (mp = 37 °C).⁹

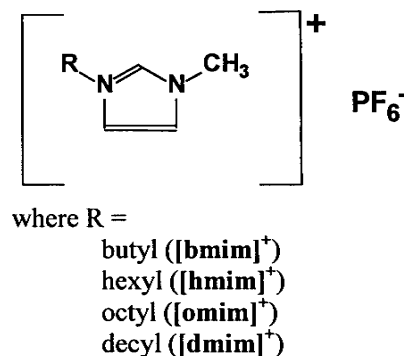


Fig. 1. One type of structural variation in ionic liquids.

Recently, RTIL have been identified in which the anion is stable to moisture and imparts water immiscibility as well, hence rendering them capable of forming a two-phase system with aqueous media.^{3,7,10} (When contacted with water, the RTIL forms the heavy, lower phase, while the aqueous phase is the light, upper phase.) The anions reported in this category include AsF₆⁻, PF₆⁻, BF₄⁻, triflate (CF₃SO₂⁻), nonaflate (CF₃(CF₂)₃SO₂⁻), bis(triflyl)amide ((CF₃SO₂)₂N⁻), trifluoroacetate (CF₃CO₂⁻), and heptafluorobutanoate (CF₃(CF₂)₃CO₂⁻).^{8,10}

Using a simple indicator dye, thymol blue, we have recently demonstrated a) reversible pH-dependent liquid/liquid partitioning, b) the use of CO₂(g) and NH₃(g) to activate the 'proton switching' of phase preference, c) that structural variation within the RTIL ions may be utilized to fine-tune partitioning behavior, and d) solid/liquid separations are possible with low melting ionic liquids. In addition, we have shown how simple ionizable metal ion extractants (e.g., PAN and TAN) may be utilized to extract metal ions in a reversible fashion, a necessary condition for efficient stripping.¹¹

pH dependent partitioning

We have investigated the partitioning of thymol blue as a function of aqueous phase pH for the [Rmim][PF₆] RTIL in Fig. 1. Qualitatively, the partitioning of thymol blue's three forms between the aqueous (top) and ionic liquid (bottom) phases can be followed by the color changes, thus at low pH thymol blue exists in its red form as a neutral zwitterion and prefers the RTIL phase. As the pH is increased, the yellow monoanion forms with some detectable increase in concentration in the aqueous phase. The blue dianion, above pH = 10, partitions quantitatively to the aqueous phase.

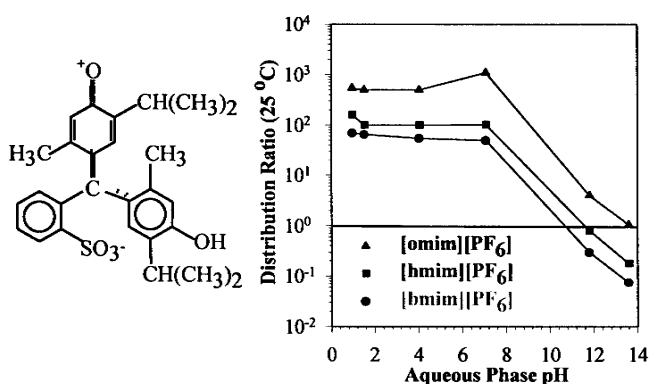
Structural Fine-Tuning of Solvent Behavior

Quantitative analysis of the partitioning of thymol blue was carried out using [bmim][PF₆], [hmim][PF₆], and [omim][PF₆]. The subtle differences in the distribution of the solute in the three ionic liquids is shown in Fig. 2. Although the general trend is the same in each RTIL, distribution ratios increase with increasing length of the alkyl substituent on the cation, with differences in distribution ratios of over an order of magnitude. Even phase preference for specific solutes can be engineered into these designer solvents.

Solid/Liquid Separations

The decyl derivative, [dmim][PF₆], is a solid at room temperature, but when heated just above its melting temperature in the presence of an acidic aqueous solution containing thymol blue, the dye immediately partitions to the RTIL phase. Separation of the RTIL phase, followed by crystallization at reduced temperature leads to pure [dmim][PF₆] crystals and deposits of the dye. This material can be easily removed from the crystals by

washing with pH = 13 NaOH.



Reversible Metal Ion Extraction

An additional challenge facing the use of RTIL in SX is the ability to reversibly and selectively extract metal ions. Hydrated metal ions show no preference for RTIL,¹¹ as expected by analogy to hydrophobic organic diluents. Thus, as in SX, extractants are needed which dehydrate and complex the metal ion providing a more hydrophobic environment. In addition the extractant must remain in the RTIL phase over the range of conditions employed in both extraction and stripping.¹²

Fig. 2. Distribution ratios of thymol blue in [Rmim][PF₆] vs. pH.

Two common transition metal ion extractants, PAN and TAN, remain in the RTIL phase from pH 1-12 in all of the RTIL discussed here. These ligands are known to coordinate transition metals through the azo and deprotonated phenolic groups. Protonation of the phenol oxygen releases the coordinated metal ion, thus raising the pH enhances extraction, lowering the pH facilitates stripping.

FUTURE NEEDS

Despite the need for VOC replacement technologies and the promise of RTIL to deliver new green processes, development of industrial technologies to utilize the unique properties of RTIL as solvents is hampered by lack of fundamental data (e.g., physical properties, toxicity, solubility data, comparators to traditional solvents, etc.). Direct comparison of RTIL to specific organic solvents, or demonstration of techniques which allow use of the cumulative knowledge in a particular field could dramatically expand their potential usage and speed the introduction of these potentially 'green' solvents into sustainable industrial processes. All of these will be needed to educate potential users and overcome the inherent barriers to new technologies, but the current emphasis on sustainable development may be just the catalyst needed to see these new technologies to fruition.

REFERENCES

1. *The Montreal Protocol on Substances that Deplete the Ozone Layer*; United Nations Environment Program (UNEP): Nairobi, Kenya, 1987.
2. Speight, J.G. *Environmental Technology Handbook*; Taylor and Francis: Washington, DC, 1996.
3. Freemantle, M. "Designer solvents - Ionic liquids may boost clean technology development," *Chemical & Engineering News* **1998**, 76, June 30, 32.
4. Dyson, P.J.; Grossel, M.C.; Srinivasan, N.; Vine, T.; Welton, T.; Williams, D.J.; White, A.J.P.; Zigras, T. "Organometallic Synthesis in Ambient Temperature Chloroaluminate(III) Ionic Liquids. Ligand Exchange Reactions of Ferrocene," *J. Chem. Soc., Dalton Trans.* **1997**, 3465.
5. Chauvin, Y.; Musmann, L.; Olivier, H. "A Novel Class of Versatile Solvents for 2-Phase Catalysis - Hydrogenation, Isomerization, and Hydroformylation of Alkenes Catalyzed by Rhodium Complexes in Liquid 1,3-Dialkylimidazolium Salts," *Angew. Chem.-Internat. Ed. Eng.* **1996**, 34, 2698.
6. Wilkes, J.S.; Levisky, J.A.; Wilson, R.A.; Hussey, C.L. "Dialkylimidazolium Chloroaluminate Melts - a New Class of Room-Temperature Ionic Liquids for Electrochemistry, Spectroscopy, and Synthesis," *Inorg. Chem.* **1982**, 21, 1263.
7. Huddleston, J.G.; Willauer, H.D.; Swatoski, R.P.; Visser, A.E.; Rogers, R.D. "Room Temperature Ionic Liquids as Novel Media for 'Clean' Liquid-Liquid Extraction," *Chem. Commun.* **1998**, 1765.
8. McEwen, A.B.; Ngo, H.L.; LeCompte, K.; Goldman, J.L. "Electrochemical Properties of Imidazolium Salt Electrolytes for Electrochemical Capacitor Calculations," *J. Electrochem. Soc.* **1999**, 146, 1687.
9. Holbrey, J.D.; Seddon, K.R. "Ionic Liquids," *Green Chemistry* **1999**, in press.
10. Bonhôte, P.; Dias, A.P.; Armand, M.; Papageorgiou, N.; Kalyanasundaram, K.; Gratzel, M. "Hydrophobic, Highly Conductive Ambient-Temperature Molten-Salts," *Inorg. Chem.* **1996**, 35, 1168.
11. Rogers, R.D.; Visser, A.E.; Swatoski, R.P.; Hartman, D.H. "Metal Ion Separations in Room Temperature Ionic Liquids: Potential Replacements for Volatile Organic Diluents," In *Metal Separation Technologies Beyond 2000: Integrating Novel Chemistry With Processing*; Liddell, K.C.; Chaiko, D.J., Eds.; United Engineering Foundation: Washington, DC, 1999; p 139.

12. Rydberg, J.; Musikas, C.; Choppin, G.R. *Principles and Practices of Solvent Extraction*; Marcel Dekker: New York, 1992.

IONIC LIQUID/CO₂ BIPHASIC SYSTEMS

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ABSTRACT

Room temperature ionic liquids (IL's) are unique, environmentally-benign reaction media¹ because they are low viscosity liquids that exhibit no measurable vapor pressure.² However, how does one recover a low-volatility or thermally labile product from an IL? Distillation is a poor option, and liquid-liquid extraction using conventional organic solvents will lead to cross-contamination of the IL and the product. Extraction of the product into environmentally-benign carbon dioxide represents an attractive alternative, but only if (a) CO₂ swells the IL to facilitate extraction of the product and (b) the IL does not dissolve appreciably in the CO₂, in order to recover the product in pure form. Here, for the first time, we show that CO₂ can completely extract a low volatility target molecule from an IL, and most significantly, that CO₂ dissolves in the IL but the IL does not dissolve any measurable amounts in the CO₂. This unique phase behavior, which superficially resembles that of a crosslinked elastomer in contact with a solvent^{3,4}, suggests that CO₂/IL biphasic mixtures are a powerful addition to our arsenal of green solutions to chemical synthesis problems.

INTRODUCTION

While room temperature ionic liquids represent a novel class of solvents that can be used for a variety of reactions, including alkylations and acylations^{1,5}, environmentally acceptable techniques for the removal of products from the IL remain a challenge. One solution is to use another environmentally acceptable solvent to extract the products from the IL. Toward this end, Rogers and coworkers have investigated the distribution coefficients of several organic solutes between 1-butyl-3-methylimidazolium hexafluorophosphate [BMIM][PF₆] and water.⁶ The problem then becomes the removal of the products from an aqueous stream. For nonvolatile and, particularly, nonpolar organic compounds, these will be dilute streams which themselves present challenging separation problems. Here we investigate an alternative environmentally benign solvent, carbon dioxide, to extract nonvolatile and thermally labile organic compounds from an IL. CO₂ has been used extensively, both commercially and in research, for the extraction of heavy organic solutes.^{7,8} Since the solvent power of CO₂ is tunable, extracted solutes can be easily and cleanly separated from the CO₂ with simple adjustments of temperature or pressure.⁸

RESULTS

1-butyl-3-methylimidazolium hexafluorophosphate [BMIM][PF₆] was synthesized as described below. It is a clear liquid with a consistency roughly similar to that of mineral oil. This particular ionic liquid is stable in the presence of both oxygen and moisture. While the goal of this work is to show whether CO₂ can be used to extract a low volatility solute from an IL, it is equally important to show that there will not be significant cross-contamination of the CO₂-rich phase with the ionic liquid. This is the problem that one would expect for any typical liquid solvent. Therefore, we investigate the phase behavior of [BMIM][PF₆] with CO₂, as well as with naphthalene, a typical nonvolatile organic solute. Finally, we show that naphthalene can be extracted quantitatively from the ionic liquid at 13.8 MPa and 40°C.

Phase Behavior

Phase behavior is of primary importance in determining the potential for using CO₂ to extract nonvolatile compounds from ILs.

1. CO₂/[BMIM][PF₆]. Ideally, the IL should be almost insoluble in CO₂, yet it would be desirable if the CO₂ was reasonably soluble in the IL liquid phase, in order to decrease viscosity and eliminate mass transfer resistances in the liquid phase. The phase behavior of [BMIM][PF₆] / CO₂ at 40°C is shown in Figure 1. Replicate experiments (the squares and circles) show that the solubility of CO₂ in the IL-rich liquid phase is substantial, reaching a mole fraction of 0.6 at 8 MPa, but that the two phases do not become completely miscible even up to 40 MPa. Significantly, the composition of the CO₂-rich phase is essentially pure CO₂, as shown by the following three experiments. First, after extracting the IL with 55 grams of CO₂ at 13.8 MPa and 40°C there was no detectable [BMIM][PF₆] in the extract, indicating that the concentration is less than 1×10^{-5} mole fraction. Second, following the extraction experiment, it was found that [BMIM][PF₆] remained in the extraction vessel, further confirming that CO₂ and the IL are not miscible at these conditions. Third, the cloud points of mixtures of 7.15 mole %, 4.92 mole % and 1.31 mole % IL (the balance CO₂) at 25°C are greater than 40 MPa, which was the highest pressure accessible with our equipment. Based on this information, we postulate that the full phase diagram of 1-butyl-3-methylimidazolium hexafluorophosphate/CO₂ resembles that shown by the lines in Figure 1. Thus, significant amounts of CO₂ dissolve in [BMIM][PF₆] but the binary solution remains essentially immiscible to pressures greater than 40 MPa. This type of phase behavior is completely unfamiliar for a CO₂/normal liquid system, where significant solubility of the liquid in the CO₂-rich phase is observed. One other atypical system is water, which dissolves in CO₂ in rather modest amounts (just 0.25-0.5 mole %). However, the presence of CO₂ induces the formation of carbonic acid in liquid water, dramatically lowering its pH and, thus, greatly limiting the types of chemistry that can be performed. The low solubility of many compounds in water is another limiting factor so CO₂/H₂O systems have limited applications. As shown below, the solubility of organic solutes in the IL is quite high. The phase behavior observed for the IL/CO₂ system is more typical of that of a cross-linked polymer/solvent system.^{3,4} Unfortunately, cross-linked polymers are extremely viscous and, therefore, not suitable reaction solvents.
2. Naphthalene/IL. Naphthalene was chosen as a representative nonvolatile organic solute. It dissolves readily in [BMIM][PF₆], with a maximum solubility of 0.30 mole fraction at 40°C.
3. Naphthalene/CO₂. The solubility of naphthalene in CO₂ has been studied extensively^{9,10} and ranges from 0.013 to 0.017 mole fraction at 35°C and pressures from 12.2 to 20.4 MPa.

Extractions

A mixture of 0.12 mole fraction naphthalene in [BMIM][PF₆] was extracted with CO₂ at 13.8 MPa and 40°C. Replicate experiments shown in Figure 2 indicate a 96% recovery from a 0.0431 g sample (containing 0.00265 g naphthalene) contacted with 67 grams of CO₂ and a 94% recovery from a 0.0409 g sample (containing 0.00252 g naphthalene) contacted with 56 grams of CO₂. This near quantitative recovery compares favorably with the extraction of a similar amount (0.0032 g) of pure solid naphthalene with comparable amounts of CO₂, which is also shown in Figure 2. Thus, it is possible to quantitatively extract a nonvolatile organic solute from an IL using CO₂ without any contamination of the product with the IL.¹¹ Moreover, the dissolution of CO₂ in the IL is completely reversible - pure IL remains in the extraction vessel after the extraction of the naphthalene and after depressurization.

Methods

Materials. 1-methylimidazole (Aldrich, 99+%, redistilled), hexafluorophosphoric acid (Aldrich, 60%), and 1-chlorobutane (Aldrich, 99.5%, anhydrous) were used as received.

Synthesis. Synthesis of 1-butyl-3-methylimidazolium chloride: In a typical experiment, 0.1 moles of 1-methylimidazole (8.2 g, 8.0 ml) and 0.1 moles of 1-chlorobutane (9.2 g, 10.4 ml) were charged to a two-neck flask equipped with a dry-ice condenser. The reaction mixture was heated at 70°C for seventy-two hours while stirring vigorously under a blanket of nitrogen. After reaction, the viscous liquid was washed three times with ethyl acetate and the traces of washing solvent were removed under vacuum at 70°C. Synthesis of 1-butyl-3-methylimidazolium hexafluorophosphate: 0.1 moles of 1-butyl-3-methylimidazolium chloride (17.4 g) in 35 g of water were first charged to a flask cooled in an ice bath. Subsequently, 0.13 moles of hexafluorophosphoric acid (31.6 g 60 wt. % solution) were added dropwise to the reaction mixture while stirring vigorously. The reaction mixture was then stirred for 12 hours at room temperature. Subsequently, the ionic

liquid was separated from the reaction mixture and washed with water until neutral pH was observed in the washings, and the excess water was then removed under vacuum at 40-50°C. Results from ^1H NMR (CDCl_3): δ 8.30 (s, 1H, imidazolium ring); 7.27 (s, 2H, imidazolium ring); 4.1 (t, 2H, NCH_2); 3.72 (s, 3H, NCH_3); 1.71 and 1.15 (2m, 4H, 2CH_2); 0.73 (t, 3H, CH_3).

Phase behavior measurements. The CO_2 /[BMIM][PF₆] phase behavior was determined in three ways. First, the solubility of the CO_2 in the IL-rich liquid phase was determined at pressures to 8.3 MPa with a high pressure view cell that has been described previously.¹² Approximately 1 g of [BMIM][PF₆] was loaded into a glass cell and CO_2 slowly metered into the cell with vigorous stirring. The mole fractions of CO_2 in the liquid phase were determined assuming the vapor phase was pure CO_2 , which is clearly a good assumption in this case. The number of moles of CO_2 in the liquid phase at a given temperature and pressure were determined by difference, using the IUPAC pure CO_2 density data¹³ to obtain the number of moles of CO_2 in the vapor phase. Second, the cloud points were determined using a variable volume view cell rated to 40 MPa, as shown previously.¹⁴ Third, the solubility of the IL in the CO_2 -rich phase was determined with an ISCO 220SX high pressure extraction apparatus. A small quantity of IL was loaded onto a polyurethane foam sponge and inserted into the high-pressure chamber. The chamber was pressurized to 13.8 MPa at 40°C and allowed to equilibrate for forty minutes. Then CO_2 was flowed slowly through the extraction cell. The saturated CO_2 phase exiting the cell was depressurized through a heated restrictor and slowly bubbled through a flask of ethanol. UV-vis absorption of the collection solvent was used to determine if any IL was extracted. The IL dissolves in ethanol and has an absorption at 212 nm that follows Beer's law over concentrations from 10^{-5} to 10^{-2} M with an extinction coefficient of $4.49 \times 10^3 \text{ M}^{-1}\text{cm}^{-1}$. The solubility of naphthalene in [BMIM][PF₆] was determined by dissolving a small amount of the saturated solution in ethanol and analyzing by UV-vis spectroscopy. The saturated IL/naphthalene solution was stirred vigorously and allowed several days for full dissolution of the naphthalene solid solute.

Extractions. The extraction of naphthalene with CO_2 from the naphthalene/[BMIM][PF₆] mixture was performed with the same ISCO extractor described above. A naphthalene/[BMIM][PF₆] stock solution containing 0.12 mole fraction naphthalene was prepared and a small amount (0.0431 g) loaded onto the sponge in the extractor. The naphthalene concentration in the ethanol collection solution was determined by UV-vis spectroscopy, using the peaks at 267 nm, 276 nm and 285 nm. Naphthalene also absorbs at 212 nm, where [BMIM][PF₆] absorbs, so the absence of [BMIM][PF₆] in the CO_2 extract was confirmed with a control experiment that did not contain naphthalene, as described above.

SUMMARY

We have shown, for the first time, that CO_2 can completely separate organic solutes with low volatility from an IL without any contamination of the extract with the IL solvent. CO_2 dissolves in the IL liquid phase but the IL does not dissolve in the CO_2 . Thus, IL/ CO_2 biphasic systems offer an exciting new environmentally benign solution for chemical synthesis and separation problems.

ACKNOWLEDGEMENTS

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LITERATURE CITED

1. Chauvin, Y. and Olivier-Bourbigou, H. *Chemtech* **25**(9), 26-30 (1995).
2. Seddon, K.R. *J. Chem. Tech. Biotechnol.* **68**, 351-356 (1997).
3. Moerkerke, R., Koningsveld, R., Berghmans, H., Dusek, K. and Sole, K. *Macromolecules* **28**, 1103-1107 (1995).
4. Moerkerke, R. *et al. Macromolecules* **31**, 2223-2229 (1998).
5. Dullius, J.E.L. *et al. Organometallics* **17**, 815-819 (1998).
6. Huddleston, J.G., Witlauer, H.D., Swatoski, R.P., Visser, A.F & Rogers, R.D. *Chem. Commun.*, 1765-1766 (1998).
7. Brennecke, J.F. *Chem. Ind.* No. 21, 831-834 (1996).
8. McHugh, M.A. and Krukonis, V.J. *Supercritical Fluid Extraction, Principles and Practice*, 2nd Ed., Stoneham, MA: Butterworth-Heinemann, 1994.
9. McHugh, M. and Paulaitis, M.E. *J. Chem. Eng. Data* **25**, 326-329 (1980).
10. Sako, S., Ohgaki, K. and Katayama, T. *J. Supercrit. Fluids* **1**, 1-6 (1988).
11. Blanchard, L.A. *et al. Nature* **399**, 28 (1999).
12. Huie, N.C., Luks, K.D. and Kohn, J.P. *J. Chem. Eng. Data* **18**, 311-313 (1973).

13. Angus, S., Armstrong, B., de Reuck, K.M., Eds. *International Thermodynamic Tables of the Fluid State: Carbon Dioxide*; Pergamon Press: Oxford, 1976.
14. Super, M., Beckman, E.J. *J. Chem. Eng. Data* **42**, 664-670 (1997).

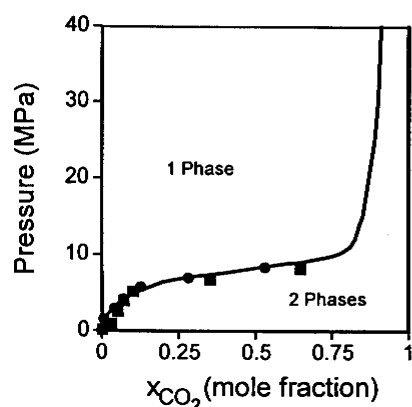


Figure 1. Schematic phase diagram of CO₂ and 1-butyl-3-methylimidazolium hexafluorophosphate [BMIM][PF₆], including data for the solubility of CO₂ in the IL at 40°C (squares and circles). Significant amounts of CO₂ dissolve in the [BMIM][PF₆] liquid phase but there is no measureable amount of [BMIM][PF₆] in the CO₂ vapor phase.

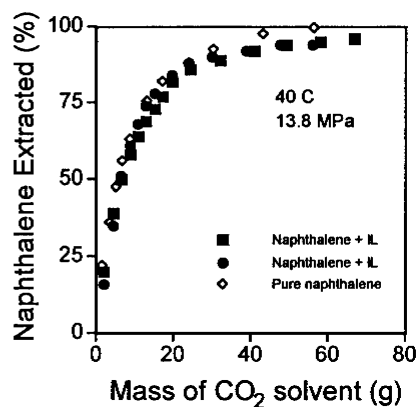


Figure 2. Extraction of naphthalene from a [BMIM][PF₆]/naphthalene liquid mixture using CO₂ at 40°C and 13.8 MPa. Essentially all of the naphthalene can be removed from the [BMIM][PF₆] without any contamination with [BMIM][PF₆]. For comparison, extraction of a pure naphthalene sample is shown on the graph, as well.

ENANTIOSELECTIVE EPOXIDATION OF OLEFINS IN SUPERCRITICAL CARBON DIOXIDE

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ABSTRACT

The use of supercritical CO₂ as a benign solvent for homogeneous catalysis of olefin epoxidation is explored. Mo(CO)₆ leads to clean epoxidation with excellent reactivity. A new class of vanadium salen catalysts shows clean epoxidation with high turnover numbers using t-BuOOH as oxidant, with good diastereoselectivity but no enantioselectivity. Manganese salen complexes show good enantioselectivity but require the novel C₆F₅I=O as oxidant.

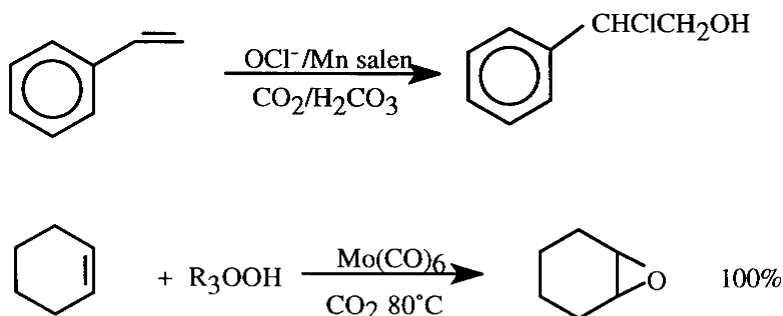
INTRODUCTION

In recent years the concept of environmentally benign, or "green" chemistry has shifted the focus of pollution reduction from end-of-pipe remediation to minimization of environmental problems at the source.¹ Our goal is to develop supercritical CO₂ (sc CO₂) as an environmentally benign solvent in selective organic oxidation reactions, with particular emphasis on homogeneously catalyzed oxidations. Since most selective oxidations are performed using aromatics, organic acids or chlorinated alkyls as solvents, introduction of sc CO₂ as a replacement would be an important step to sustainable technology. Sc CO₂ is an outstanding solvent for sustainable technology because it is completely non toxic, non corrosive, easily handled, cheap and recyclable. It is particularly suitable for homogeneous oxidations because it is inert to oxidation itself and is completely non-coordinating toward the metal center.² An experimental protocol has been developed for the rapid, simple screening of a variety of catalysts, substrates and conditions. Two specific oxidation reactions will be investigated, epoxidation of olefins and selective oxidation of alkyls. These are thought to be excellent test case studies because both are of tremendous industrial importance, and current procedures for each often require undesirable solvents. Also both reaction types are somewhat demanding in terms of selectivity, although for different reasons. Both reactions require homogeneous metal catalysts for sufficient selectivity and reactivity. There are two aspects to such

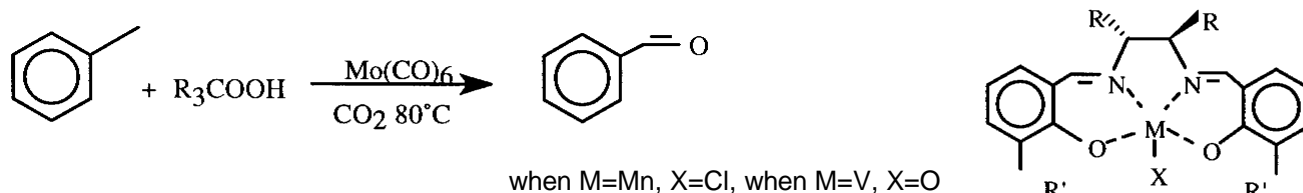
systems, the terminal oxidant and the metal catalyst and both will be investigated herein.

RESULTS AND DISCUSSION

Our initial efforts involved selective oxidation of alkenes using organic hydroperoxides (t-BuOOH) in supercritical CO₂. When Mo(CO)₆ is added, alkenes are oxidized rapidly and cleanly to epoxides if no water is present.³



We were also gratified to find that we could obtain excellent regioselectivity with these epoxidation reactions. The fact that no reaction takes place below 80°C, and the presence of an induction period, suggests that CO dissociation, followed by oxidation of the molybdenum center to a peroxy complex, is an important first step. The use of a labile complex Mo(CO)₅L where L is a labile alkene ligand leads to rapid reaction at 50°C, which supports this postulate. A range of cyclic, polycyclic and acyclic alkenes can be epoxidized cleanly. However, trans acyclic alkenes either show little or no reactivity, suggesting that steric factors play an important role in coordination of the substrate to the catalytic metal center. In addition when the alkenes contain a phenyl group directly attached to the olefin, only cleavage is observed with formation of aldehydes. However, this cleavage only occurs when an aromatic group is attached directly to the alkene. Thus it appears that Mo(CO)₆ is an excellent catalyst precursor for the selective oxidation of alkenes to epoxides or diols in supercritical CO₂. One potentially important side result is the observation that alkyl aromatics can be oxidized selectively the aldehyde using Mo(CO)₆ as the catalyst precursor. The yield is low but the selectivity is excellent.



We are also investigating the reactivity of various vanadyl catalysts, particularly a new series of vanadyl salen complexes.

These proved to have satisfactory solubility in CO₂ and displayed excellent reactivity to epoxidation of a wide variety of allylic alcohols and aromatic alkenes.⁴ We were able to observe almost quantitative conversion and substantial diastereoselectivity for these epoxidations. Reaction conditions are mild and products are generally very clean (Table 1). The catalyst stays intact and turnover numbers exceed 5000.⁵ The use of metal salen complexes is particularly encouraging because the chemistry of these ligand systems is well developed and it is relatively simple to modify the framework, leading to highly soluble and selective catalysts. In an attempt to induce asymmetry, we isolated and resolved forms of the asymmetric vanadyl complexes and hoped to use them to induce enantioselectivity. However no enantioselectivity was observed using this catalyst.

There are several catalytic systems which induce asymmetric oxidation in more conventional solvents, and we have selected the manganese salen systems developed by Jacobsen and co-workers, for our initial investigations. These are neutral compounds with heavy hydrocarbon functionality which suggests that they might be soluble in CO₂ as well. In addition Jacobsen typically uses methylene chloride as a solvent, so it would seem especially desirable to be able to extend this system to the more benign CO₂.

The choice of oxidant is somewhat problematic. The conventional oxidant is OCl⁻, but the increased acidity of the CO₂ leads to clean formation of hydrochlorinated products in good yield.

These selective chlorinations are industrially important reactions and this chemistry certainly deserves further attention.

Table 1. Epoxidation of Alkenes Using Vanadyl Salen and t-BuOOH in SC CO₂

Alkene	Product	Yield
		64%/70% erythro
		47%/72% erythro
		76%/69% erythro
		86%
		50%
		57%
		99%
		33%
		36%

We tried using R₃COOH as an oxidant. However, the high oxidation potential of the Mn(III) center of the catalyst leads to oxidation of the terminal hydrogen with formation of peroxy radical which substitutes a to the olefin in high yield.

One oxidant that appeared promising was iodosyl benzene, but the oxidant is insoluble in sc CO₂ and thus unreactive. We found however that addition of small amount of co-solvent leads to sufficient increase in solubility to provide good yields of epoxidized product using resolved Mn(III) salen catalysts. For example addition of 5% heptane is sufficient to induce clean epoxidation of styrene.

Enantioselectivity was observed but the ee was low (25%). Based on these promising results, we examined other oxidants. The most promising to date is C₆F₅I=O, which is sufficiently soluble to provide good oxygen transfer capability in sc CO₂. In the presence of asymmetric Mn salen catalysts, we obtained clean epoxidation with very good enantioselectivity, up to 89% in the best cases (Table 2).⁶ Thus for the first time we observed *asymmetric epoxidation of olefins in sc CO₂ with ee's comparable to those in conventional solvents*. Variation of the density of the solvent does not lead to change in ee. However we do observe that the chemical yield increases with lower density solvent. The ee's do increase at lower temperature (5°C) at the expense of some chemical yield.

Table 2. Epoxidation of Olefins in sc CO₂ with C₆F₅I=O Using Asymmetric Mn Salen Catalyst

Olefin	init psi	T °C	% yield	ee in sc CO ₂ ^a	ee in CH ₂ Cl ₂ ^b
a-methylstyrene	3000	25	32	41	30
"	2000	25	73	40	"
"	1000	25	91	41	"
"	3000	5	15	56	"
cis b-methylstyrene	3000	25	12	58	84
triphenylethylene	3000	25	18	36	9
trans-stilbene	3000	25	16	22	33
1-phenylcyclohexene	3000	25	7	52	56
1,2-dihydronaphthalene	3000	25	35	85	78

SUMMARY

Supercritical CO₂ is a suitable solvent for selective epoxidation of olefins. The choice of oxidant is dependent on the particular catalysts. The metal salen complexes are suitably soluble and selective catalysts in sc CO₂. t-BuOOH is satisfactory as an oxidant in the presence of V(IV) but leads to unselective radical chemistry in the presence of Mn(III). However the novel oxidant C₆H₅I=O does show promising enantioselectivity for asymmetric epoxidation of olefins.

REFERENCES

1. "Green Chemistry: Designing Chemistry for the Environment" P.T. Anastas, T.C. Williamson Eds. ACS Symposium Series vol. 626 American Chemical Society, Washington DC, 1996.
2. D.A. Morgenstern, R.M. LeLacheur, D.K. Morita, S.L. Borkowsky, S. Feng, G.H. Brown, L. Luan, M.F. Gross, M.J. Burk, W. Tumas, in ref 1, pg 132.
3. Haas, G.R.; Kolis, J.W. *Organometallics* **1998**, 17, 4454.
4. Haas, G.R.; Kolis, J.W. *Tet. Letts.* **1998**, 39, 5923.
5. Haas, G.R.; McFadden, E.; McKay, S.; Flowers, A.M.; Kolis, J.W. *J. Molecular Catalysis A* submitted.
6. Haas, G.R.; McKay, S.; Kolis, J.W. *J. Chem.Soc. Chem. Commun.* **1999** submitted.

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**ENVIRONMENTALLY
BENIGN PROCESSING**

RADIATION CHEMISTRY: THE BASIS FOR AN INHERENTLY GREEN PROCESS TECHNOLOGY

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Abstract

In using ionizing radiation generated from electron beam accelerators and/or using photoinitiated reactions started by high intensity ultra-violet light, industry has eliminated volatile organic compounds (VOCs) from coatings, inks and adhesives. Such processes have also been found to be energy efficient and to minimize wastes, conserving both energy and materials. Large scale process studies have indicated that ionizing radiation can also be used to precipitate SO₂/NO_x from stack gases and to dehydrohalogenate toxic halocarbons found in wastewater and in soils. While recognized for its environmental benefits by organizations such as the EPA, the IAEA and NSF, industrial acceptance of such inherently green processes based on radiation chemistry has been slowed by a tendency in US industry to conserve capital in plant and equipment rather than make fundamental changes in process technology. Case studies will be presented to illustrate the mechanisms involved and the resultant economic and environmental benefits.

Key words

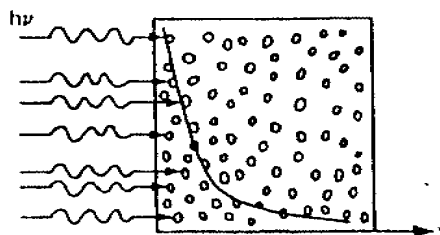
radiation chemistry; electron beam processing; ultra-violet curing; environmental benefits; industrial impact; volatile organic compound (VOC) elimination; environmental remediation.

Introduction

Radiation chemistry embraces a broad scope of scientific and technical inquiry. However, except for the selected use of gamma emission from ⁶⁰Co for medical device sterilization and its emerging use for food treatment, industry does not utilize radioactive sources. Industrial radiation processing relies primarily on two electrically generated radiation sources: accelerated electrons and photons from high intensity ultraviolet lamps. Accelerated electrons have the ability to penetrate matter, being stopped only by mass. In contrast, high intensity ultra-violet generates primarily surface effects.



Electron Beam Penetration

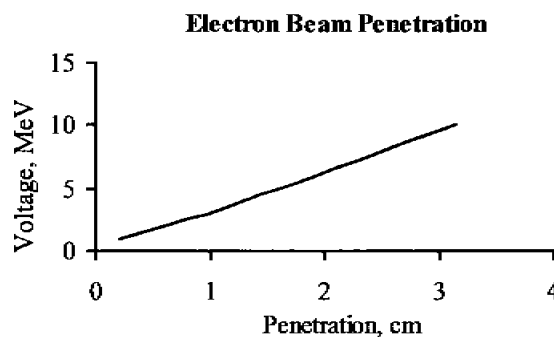


Ultra-violet Light Penetration

There are over 1000 high current electron beam accelerators now in industrial use, ranging in voltage potential from 70 kV up to 10 MeV. With electron penetration being proportional to acceleration voltage, the lower voltage accelerators find use in surface curing and the crosslinking of polymeric films; mid-voltage accelerators are used to crosslink the jacketing on wire and cable and in the manufacture of heat shrink tubing and to partially crosslink tire components. High voltage 10 MeV accelerators are being used in the crosslinking of matrix materials in carbon fiber composites and are being evaluated for food processing applications and medical device sterilization.¹ Given their significantly lower capital costs, there are well in excess of 100,000 high intensity ultraviolet units now in industrial use. Their applications deal mainly with the surface curing of inks, coatings and adhesives. These units typically operate in the 200 to 450 nm range, with lamp intensities as high as 240 watts/cm of lamp length.

VOC Elimination

The increased industrial acceptance of high intensity ultra-violet light (UV) processing and the use of low voltage electron beams (EB) have been stimulated by the Clean Air Act Amendments of 1990. Historically, formulations for inks, coatings and adhesives have relied on the use of polymeric resins dissolved



in volatile organic solvents in order to reduce viscosity needed for application. Systems with comparable finished properties have been developed based on compositions of non-volatile monomers and oligomers, typically <10,000 in molecular weight. For the most part, the chemistries involved rely upon the vinyl termination of acrylated moieties. There are, for example, acrylate terminated urethane, polyester and epoxy oligomers. Required application viscosities are achieved by diluting such oligomers with appropriate monomers or monomer combinations without the use of volatile organic solvents. Such liquid materials are converted to dried inks or coatings, having all of the functional properties of the more traditionally used solvent borne systems, upon exposure to an electron beam or, when formulated with photoinitiator compounds, to ultra-violet light, but without the dependence on VOCs. The dominant mechanisms involved are free radical conversion of double bonds to form higher molecular weight or fully crosslinked polymeric materials.²

The merits of such systems have been noted by EPA Administrator Browner in her Senate testimony of February 12, 1997. This past November (1998), the South Coast Air Quality Management District (SCAQMD), which is responsible for air quality in the Los Angeles basin, has officially recognized UV/EB curing as an environmentally friendly process and exempted such processes from some of its permitting requirements.

In some states, such as New York, there has been a confluence of environmental concern through enforcement and economic support for environmentally friendly or "green" process technologies. The New York State Energy Research and Development Authority (NYSERDA) has funded several projects involving UV/EB processing. In one case, a small, family owned business in the Catskills producing a common wood product, brush blocks, that is the base of push brooms, received around \$160,000 in financial assistance to obtain a spray coating/UV curing process line. This firm was thus able to eliminate its use of 20% solids nitrocellulose lacquers and convert to UV processing. This not only eliminated VOCs as an air pollutant, but also reduced production concerns over solvent vapors which irritated workers, the need for segregated coating rooms and facilities, and the like. However, the real bonus in converting to UV curing in coating these small wood products was found in enhanced production efficiency. This particular process line is capable of instant start-up and shutdown, thereby minimizing any process waste. Because the UV cure is nearly instantaneous, production rates were increased over six fold. A full pallet of coated wooden pieces, which would have taken over half a day to coat and dry using a solvent system and infrared heating, was finished in less than 45 minutes. While the base cost for a UV curable coating was considerably more than for a traditional solvent borne lacquer, on an applied cost basis, there was an actual savings on the cost per coated part, which included not only materials, but labor savings as well.³

Energy Efficiency

Besides state and regional utility related organizations, the Electric Power Research Institute (EPRI) has also been supportive of the electrotechnologies of UV/EB processing. Ultra-violet and electron beam processing represent a clean and efficient use of electrical power. In contrast to water borne technologies, process systems based upon radiation chemistry represent a truly "green" technology. All water based processes, whether used in converting industries to reduce dependence upon organic solvents and their emissions or even in synthesis schemes, are inherently energy inefficient. Ultimately, water must be driven off to produce a dried product or material.⁴

Energy Needed to Dry/Cure Coatings

Coating System	Solvent Based	Water Based	EB Curable
	177 cal/gram	810 cal/gram	7 cal/gram

Environmental Remediation

One of the legacies of industrial development has been the heretofore cavalier disposal of halocarbons, whether used as degreasing solvents in metal processing, as non-flammable insulating oils in electrical transformers or purposely used as defoliants as in dioxin. Studies, funded primarily by the National Science Foundation, have shown that ionizing radiation from an EB source can dehydrohalogenate these materials, leaving a less hazardous organic material and a soluble halide. Studies were conducted using a full-scale 1.5 MeV electron beam at the Miami Dade waste treatment facility. Lower voltage, self-shielded transportable electron beams were developed and placed in tractor-trailers for on-site demonstrations of soil and water remediation. While technically feasible, this use of radiation processing has not been a commercial success. Environmental engineers seem to be more familiar with alternative processes.⁵

Stack Gas Treatment

Countries dependent on coal as their primary fuel source, such as Poland, have investigated the use of EB treatment of stack gases to eliminate SO₂/NO_x emissions from power plants. When irradiated in the presence of a small amount of ammonia, these undesirable flue gases form a white precipitate that can be removed from the gas stream and collected for other use, such as fertilizer. Engineering details for a semi-works facility using two double window 800 kV accelerators in tandem have been completed. Around \$20,000,000 in funding for this project has been facilitated by the International Atomic Energy Agency.

Summary

Radiation chemistry has formed the basis for a number of environmentally friendly or "green" industrial process technologies. Commercial success has been found in the elimination of volatile organic compounds for printing and coating processes. Technical feasibility has been demonstrated in water, wastewater and soil remediation. Scale-up is underway in the radiation treatment of stack gases. Radiation initiated synthesis can proceed at rapid rates with minimal need for catalysts and the problems of catalyst removal and disposal. Yet, this venue remains largely under explored. Not only does the societal apprehension of the term "radiation" thwart some of these developments, but more so is a lack of inclusion of this form of energy transfer in most academic regimes and curricula. Radiation is, after all, as natural as sunlight itself.

References

1. Bly, J. "Electron Beam Processing", International Info. Assoc., Yardley, PA, 1988.
2. "UV/EB Curing Primer", RadTech International North America, Bethesda, MD, 1991.
3. Larson, S. and Berejka, A. "A Clean Sweep - UV Curing of Small Wood Products" in *The RadTech Report*, May/June 1999.
4. Berejka, A. "Irradiation Processing in the '90's" in *Radiation Physics and Chemistry*, vol. 46, nos. 4-6, pages 429-437, 1995.
5. Cooper, Curry, O'Shea. "Environmental Applications of Ionizing Radiation", John Wiley & Sons, Inc., New York, NY, 1998.

TOWARDS THE DEVELOPMENT OF A LIGHT INDUCED CHEMICAL SWITCH: LIGHT INDUCED PARTITIONING OF SPIROPYRANS

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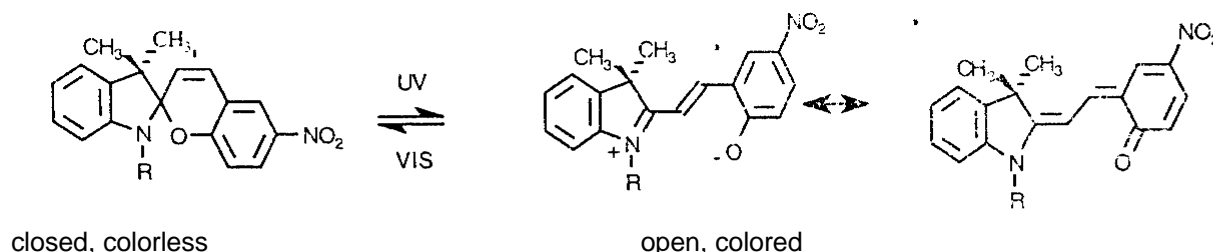
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INTRODUCTION

There are a wide variety of light induced processes which take place in plants and other organisms. Vision¹ and photosynthesis² are two fundamental processes that are triggered by optical signals. In all light activated processes, there is a chromophoric group which absorbs light and then undergoes a chemical transformation. For a chromophore to be a chemical switch, it should be possible to generate two distinct states that are interconvertible using optical signals. These chromophores can be incorporated into polymers, membranes, etc. to make them photo responsive. Some of the applications envisaged for these optical switches are in the area of information storage³, controlled drug release, separations, etc.

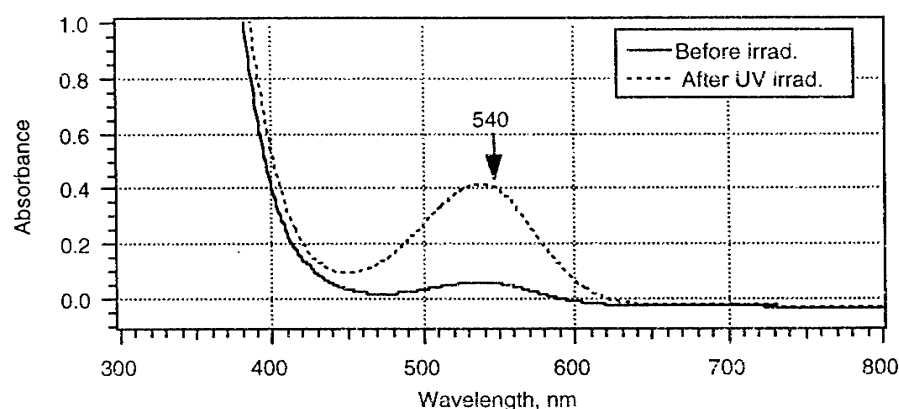
Spiropyrans are a class of compounds which are photochromic in nature.^{4,5} It has two states with different absorption spectra and the interconversion can be carried out using radiation in the UV and visible regions. In

these compounds, there is typically one state that is more thermodynamically stable than the other. The stable state of most spiropyrans is the closed, colorless form and the less stable state is the open, colored, merocyanine form. This process is represented in Scheme 1.



Scheme 1. Light induced transformation of spiropyrans between its states.

Since the colored and colorless states of spiropyrans are distinct chemical species with different polarities, they should undergo different chemical reactions. It is with this objective that the present investigation is undertaken.



Three different spiropyrans are synthesized. The difference in partition coefficients in a two phase system as a function of the wave-length of irradiation and pH are determined.

RESULTS

The absorption spectra of the two forms are shown in Figure 1.

Figure 1. Absorption spectra of the open and closed forms

The substituents are $-\text{CH}_3$, $-(\text{CH}_2)_3\text{-COOCH}_3$ and $-(\text{CH}_2)_3\text{-COOH}$, in the three spiropyrans studied. The spiropyran is dissolved in toluene and a two phase system set up with aqueous phase at pH's 2,4,6,8 and 10 respectively. Mixing is done under irradiation and the amount of spiropyran partitioned into the aqueous phase is determined from the difference in the absorbances. Mixing is done again under UV irradiation to convert the spiropyran into the open form and the amount partitioned is determined again. From these, the partition coefficients are determined. The data obtained are shown in Table 1.

Table 1. Partition coefficients when aqueous phase is at pH 2

Compound	K (aq/tol)				
	Vis - irradi.	UV -1	Vis -1	UV -2	Vis -2
BIPS	0	0.39	0.09	0.2	0.03
SP-ester	0	0.47	0.02	0.41	0.02
SP-acid	-	-	-	-	-

The spiropyran with the acid substituent seemed to undergo degradation at pH 2. However, the partitioning differences was seen at pH 4 and 6. These data are shown in Table 2.

Table 2. Partition coefficients of SP - COOH at pH 4 and 6

pH	K (aq/tol)				
	Vis - irradi.	UV -1	Vis -1	UV -2	Vis -2
4	0	0.22	0.01	0.27	0.05
6	0.1	0.27	0.1	0.22	0.1

CONCLUSIONS

Spiropyrans undergo reversible ring opening and closure upon irradiation. There is a significant difference in the partitioning of spiropyrans under UV and visible light irradiation conditions. This is attributed to differences in the polarities of the two states. By varying the substituents on the ring, these compounds can be tailored for specific purposes.

REFERENCES

1. L. Stryer, *Am. Rev. Neurosci.* 1986, 9, 87.
2. G. Feher, J.P. Allen, M. Okamura, D.C. Rees, *Nature* 1989, 339, 111.
3. Z.F. Liu, K. Hashimoto, A. Fujishima, *Nature* 1990 347, 658.
4. Photochromism (Ed.: G.H. Brown), Wiley, New York, 1971.
5. Photochromism: Molecules and Systems (Eds.: H. Dürr, H. Bouas-Laurent), Elsevier, Amsterdam, 1990.

A CHLORINE-FREE PROCESS FOR MAGNESIUM REMOVAL FROM ALUMINUM SCRAP

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Abstract

The Albany Research Center has developed technology to recover by-product materials from aluminum scrap using engineered scavenger compounds (ESC). ESCs are structural oxides with a channel or tunnel structure that allows them to hold ions of specific sizes and charges. The scavenging reaction is easily reversible allowing the ESC to be recharged for continued use and the ion is recovered as an electrodeposit. Key features of this novel technology are:

- a) ESC systems are designed to have a high degree of selectivity for a desired ionic species.
- b) The recovered material requires little or no additional reprocessing prior to reuse.

Two current uses for the ESC technology that are described in this paper are the removal and recycle of lithium (Li) from lithium aluminum (Li-Al) alloys; and, using ESCs as a replacement for the conventional demaging (magnesium removal) technology used by the secondary casting industry. Research indicates that the ESC technology proposed for both these applications has either distinct economic and/or environmental advantages over previously employed methods of recovering metal values from aluminum scrap.

Introduction

The Albany Research Center has developed technology selectively recover metals from aluminum scrap without using chlorine (Cl₂) gas. The research is based on engineered scavenger compounds (ESC). ESCs are structural oxides designed with a specific affinity for a specific ion size and charge to selectively remove a desired species from a melt. The ESC reaction is easily reversible so that the recovered species is available for recovery and reprocessing, and the ESC is then available for reuse. Current applications for this technology include removal and recycle of high purity Li from aluminum lithium (Al-Li) alloys¹⁻³ and removal and recovery of high purity Mg from aluminum (Al-Mg) magnesium alloys⁴.

Al-Mg alloys which contain up to 3 pct Mg and must be "demaged" (have the Mg level reduced to 0.1-0.6 pct Mg before use) for use in casting alloys. The current technology available for magnesium removal offers four

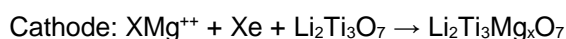
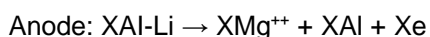
approaches: 1) oxidation of the Mg during melting of the scrap, 2) vacuum distilling of the Mg from the bulk scrap during melting, 3) reaction with chlorine (Cl_2)^{5,6}, and, 4) displacement with iron (Fe). Economic and practical considerations eliminate 2) and 4) because of requirements for additional processing steps or the requirement for expensive vacuum equipment. The chlorination process requires emission control of the fugitive chlorine compounds as well as disposal of the slags created in the process at a secured landfill. Oxidation results in the economic loss of the magnesium and additional slag disposal problems.

Because of this need, the Albany research Center has conducted very successful research to investigate the synthesis and scavenging properties of ionically conducting ceramic oxides such as lithium titanate ($\text{Li}_2\text{Ti}_3\text{O}_7$) for Li recovery from Al-Li alloy and Mg recovery from Al-Mg alloys.

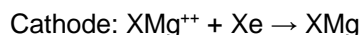
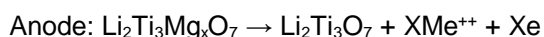
Mg Recovery

The reaction for demaging and Mg recovery from the ESC is as follows:

Mg removal from Al-Mg alloy



Mg removal from Mg-loaded $\text{Li}_2\text{Ti}_3\text{Mg}_x\text{O}_7$



The results from Mg recovery experiments are listed in table 5. Experiments were conducted using both $\text{Li}_2\text{O} \cdot 3\text{TiO}_2$ and V_2O_5 as the ESC. Other structural oxides such as WO_3 and MoO_3 may also prove to be suitable ESCs. The characteristics of the reaction were that it was fast, selective and the Mg could be recovered from the ESC by electrolysis on the stainless steel electrodes.

Table 5. Demaging Al-Mg Alloys at 550 °C (Original Mg content, 2.28 pct.)

Test Number	ESC	Mg removal, pct
1	$\text{Li}_2\text{O} \cdot 3\text{TiO}_2$	67.00
2	$\text{Li}_2\text{O} \cdot 3\text{TiO}_2$	65.25
3	$\text{Li}_2\text{O} \cdot 3\text{TiO}_2$	69.10
4	$\text{Li}_2\text{O} \cdot 3\text{TiO}_2$	73.50
5 ¹	$\text{Li}_2\text{O} \cdot 3\text{TiO}_2$	87.20
6 ²	$\text{Li}_2\text{O} \cdot 3\text{TiO}_2$	90.50
7	V_2O_5	75.70

¹Cycle 1 - ESC then recharged by electrodepositing Mg on stainless steel electrode

²Cycle 2 - ESC reused with fresh charge of scrap aluminum

Although this research is in its infancy, initial experiments have shown that it does remove Mg. The reaction is reversible and we have successfully reused the ESC for another cycle. We believe that substituting this innovative technology for the conventional chlorination technology will reduce the possibility fugitive air emissions by reducing the need for chlorine gas (Cl_2) used in this process, as well as, the amount and hazardous nature of the slag formed by the existing process.

References

1. Riley, W.D., B.W. Jong, W.K. Collins, and S.J. Gerdemann. Recovery of Li from Alloys of Al-Li and Li-Al using Engineered Scavenger Compounds. U.S. Pat. 5,324,394, Jun. 28, 1994.
2. Collins, W.K., W.D. Riley, and B.W. Jong. Hexagonal Phase Transformation in the Engineered Scavenger Compound Lithium Titanate. BuMines RI 9465, 1993, 11 pp.
3. Riley, W.D. and B.W. Jong. Engineered Scavenger Compounds; Recovery of Lithium from Lithium-Aluminum

- Alloys. Process Mineralogy XII - Applications to Environment, Precious Metals, Materials Beneficiation, Pyrometallurgy, Coal and Refractories. Edited by W. Petruk and A. R. Rule. The Minerals, Metals & Materials Society, 1994. pp 39- 52.
4. Riley, W.D. and B.W. Jong. Removal and Production of High-Purity Magnesium from Aluminum-Magnesium Alloys Using an Engineered Scavenger Compound. U. S. Pat. 5,500,100, March 19, 1996.
 5. Tiwari, B.L., Damaging Process for Aluminum Alloy Scrap. *J. Met.*, July 1982, pp.54-58.
 6. Riley, W.D., Chloride-Free Processing of Aluminum Scrap to Recover By-Product Materials. Proceedings of III International Congress Of Materials, Instituto Tecnological De Saltillo, Saltillo, Coahuila, Mexico, Oct 23-25. Pp 403-414.
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EXTRACTION OF PLATINUM GROUP METAL CHLORIDES (MCl_x^{-2}) FROM AQUEOUS HCl TO LIQUID CO_2 : A LIQUID CO_2 -ANALOG TO THE CURRENT METAL REFINING PROCESS

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ABSTRACT

Liquid carbon dioxide can be used as a replacement for organic solvents in the extraction of anionic PGM complexes from an aqueous phase. Organic solvents contaminate aqueous streams in liquid-liquid extraction. By using liquid carbon dioxide there would be no need for remediation of aqueous waste streams. In this project we use liquid carbon dioxide, and CO_2 soluble metal binding ligands to extract platinum, gold, and palladium from aqueous solutions.

INTRODUCTION

Currently, the most widely used route for purification of platinum group metals (PGM's, i.e., platinum, palladium, rhodium, iridium, gold, ruthenium, osmium) consists of mining and crushing PGM-bearing ore, then leaching the metals using an HCl/ Cl_2 biphasic mixture at elevated pressure. The resulting aqueous solution is a mixture of various metal chloride anions, including $AuCl_4^{-2}$, $PtCl_6^{-2}$, $PdCl_4^{-2}$, as well as the analogous rhodium, iridium, and ruthenium species. In addition, small amounts of a wide variety of less-valuable or value-less metals are also extracted from the ore. The various MCl_x^{-2} species are further separated via a series of solvent extraction steps. Here, a ligand (trioctyl amine for platinum, dioctyl sulfide for palladium) is protonated upon exposure to the aqueous solution, and then binds to the MCl_x^{-2} species, transporting it into the organic phase.

The current method for refining PGM's creates contact between aqueous and organic phases, and thus leads to cross-contamination. We have therefore endeavored to employ liquid carbon dioxide as the organic phase in such extractions to eliminate the waste stream deriving from organic contamination of the aqueous phase. Whereas traditional metal binding ligands dissolve in CO_2 at moderate pressures, the resulting complexes $[(LH)_2MCl_x]$ exhibit negligible solubility in CO_2 at pressures up to 6000 psi. Before designing these ligands we performed solubility studies on trioctylamine and trioctylamine bound to metal. The trioctylamine by itself was extremely soluble in carbon dioxide at moderate pressures. The complexes were not soluble in carbon dioxide therefore trioctylamine will not work for our studies and new ligands have to be synthesized.

RESULTS AND DISCUSSION

Phase Behavior

We have successfully generated highly CO_2 -soluble chelating agents. These compounds can be used to extract PGM's from an aqueous phase into liquid carbon dioxide. Single-tail, double-tail, and triple-tail amines with fluoroether or fluoroalkyl tails of various molecular weights were synthesized. The single fluorinated tail extractant was found to be soluble over a wide concentration range in liquid CO_2 at 72°F and pressures less than 1500 psi. Phase behavior studies in CO_2 also revealed that $(ligand)_2-PtCl_6$ complexes of each extractant studied were soluble in CO_2 at slightly higher pressures, therefore both the chelating agent ligand and the ligand-metal anion complex would be soluble in carbon dioxide. As the MW of the ligand increased, the two-phase boundary moved to higher pressures. For example, the fluoroalkyl single-tailed amine chelating agent is soluble in carbon

dioxide at a concentration of 1 wt% at 1000 psi while the platinum complex is soluble at 2300 psi.

The double tail modified extractant was found to be soluble in liquid-CO₂ at 72° F at pressures between 1000-5000 psi. A platinum complex formed with one of these chelating agents has been shown to be more soluble in carbon dioxide than the chelating agent. For example, the fluoroalkyl double-tailed amine chelating agent is soluble in carbon dioxide at a concentration of 2 wt% at a pressure of 1800 psi while the platinum complex is soluble at 1097 psi. Similar behavior was observed by Yazdi and Beckman. Lead-fluoroether dithiocarbamate complex was more soluble than the fluoroether dithiocarbamate by itself. But on a mole percent basis the unbound fluoroalkyl double tail is more soluble than the unbound, which is consistent with what was seen with the single-tail. Phase behavior studies of the double tail fluoroalkyl platinum complex and double tail fluoroalkyl gold complex were compared. We found that the platinum-ligand complex is less soluble than the gold-ligand complex.

Efficiency Factors

Liquid vial studies were performed to determine the efficiency factor. The efficiency factor indicates whether the ligand exhibits good binding or not. The fluorinated chelating agent was dissolved in 1,1,2 trichlorotrifluoroethane. (1,1,2 trichloro trifluoroethane is an ambient pressure "screening" liquid used to assess the viability of the chelating agent). A designated amount of aqueous metal chloride solution (Pt, Au, in HCl) was then added to the vial. The solution was then mixed and allowed to equilibrate for 12 hours. The top phase (aqueous phase) was then sampled and analyzed via assay and spectrophotometric determination (Onishi, H.,1978). Recently we have also used Inductively Coupled Plasma Atomic Emission Spectrometry (ICP-AES) to analyze the top phase. We use this data to determine the degree of metal extracted, E.

The efficiency factors of these compounds for platinum extraction were 0.177 for the fluoroalkyl single-tail amine (583 MW), and 2.74 for the fluoroalkyl double-tail amine (937 MW). In these figures $E/(1-E)$ vs. $(R-2E)^2$ the E is the degree of metal extracted and the R is the ratio of metal to chelating agent used. The slope of this graph is the efficiency factor. The higher the efficiency factor the better the binder it is. We noticed that the tail had an effect on the binding of the metal. The tails were added to increase solubility; we had no idea that they would have an effect on binding. The same phenomena occurred in the fluoroether tails.

Extraction from the Aqueous Phase into 1,1,2 trichlorotrifluoroethane

Efficiency factors indicated that strong and nearly complete binding of the metals would occur. The extraction results provided a measure of how much of the bound metal could be recovered into the 1,1,2-trichlorotrifluoroethane. Single-stage extractions of the PGM's into a 1,1,2 trichlorotrifluoroethane phase (a screening liquid for ambient pressure experiments) from the aqueous phase were completed. The fluoroalkyl single-tail chelating agent extracted 70% of the platinum from the aqueous phase. The fluoroalkyl double-tail amine extracted 93% of the platinum at 93% (chelating agent:platinum ratio of 4:1). The fluoroether single-tail extractant recovered 54% of the Pt (chelating agent:platinum ratio of 3:1). An extraction in carbon dioxide using the fluoroalkyl double tail amine was performed. This agent extracted 88% of the platinum into the carbon dioxide. Extractions with other PGM's, multiple stage extractions in columns, and extractions into carbon dioxide are currently being conducted

SUMMARY

Consequently, we have designed and synthesized a series of highly CO₂-soluble analogs to the metal-binding ligands currently used by the PGM-refining industry. We have measured efficiency factors for various ligands and platinum, palladium, and gold, and have found that the structure of the CO₂-philic part of the ligand strongly affects the efficiency factor, thus allowing us to engineer selectivity via ligand molecular structure. Finally, we have noted that the phase behavior of the ligand-metal complex is a function of both ligand structure and the identity of the metal, opening the possibility for separations based on both pressure and ligand selectivity. A model trial in carbon dioxide showed that 87.5% of platinum was extracted from a platinum solution using a 4:1 chelating agent to metal ratio.

ACKNOWLEDGEMENTS

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REFERENCES

1. Marczenko, Z.; Spectrophotometric Determination of Elements, (1976), Halsted Press, New York, NY.

2. Onishi, H.; Determination of Traces of Metals, (1978), John Wiley & Sons, New York, NY.
3. Yazdi, A.V.; Beckman, E.J. "Design, Synthesis, and Evaluation of Novel, Highly CO₂-Soluble Chelating Agents for Removal of Metals" *Ind. Eng. Chem. Res.* **1996**, 35, 3644-3652,
4. Yazdi, A.V.; Beckman, E.J. "Design of Highly CO₂-Soluble Chelating Agents. 2. Effect of Chelate Structure and Process Parameters on Extraction Efficiency". *Ind. Eng. Chem. Res.* **1997**, 36, 2368-2374.

CARBON DIOXIDE-ASSISTED AEROSOLIZATION AND BUBBLE DRYING FOR PHARMACEUTICAL SYNTHESIS AND FINE PARTICLE FORMATION

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ABSTRACT

A new environmentally benign technology has been developed for the production of fine particles of pharmaceuticals and other materials. This technique utilizes the relatively high solubility of supercritical carbon dioxide in water as a means to aerosolize aqueous solutions of therapeutic drugs. Through mixing of the two fluids, an emulsion of the aqueous drug solution and supercritical or near-critical liquid carbon dioxide is created and subsequently expanded through a restrictor to yield a fine, dense aerosol that can be directed into a drying chamber to produce fine particles. These particles have diameters in the 0.5 - 5 μm size range, which makes them suitable for treatment of lung-related illnesses. The particles are typically amorphous and spherical, but can possess various morphologies, and can be solid or hollow. Efficient aerosolization of the aqueous solution due to the expansion of dissolved CO₂ allows for more rapid drying of the droplets at lower temperatures than can typically be achieved with conventional spray-drying techniques, an advantage in pharmaceutical processing. This technology is applicable to a wide range of materials and can replace processes utilizing organic solvents and chlorofluorocarbons. Examples of fine drug or excipient particles produced by this method include albuterol sulfate, cromolyn sodium, tobramycin sulfate, rhDNase, sodium chloride, lactose, and various protein formulations.

INTRODUCTION

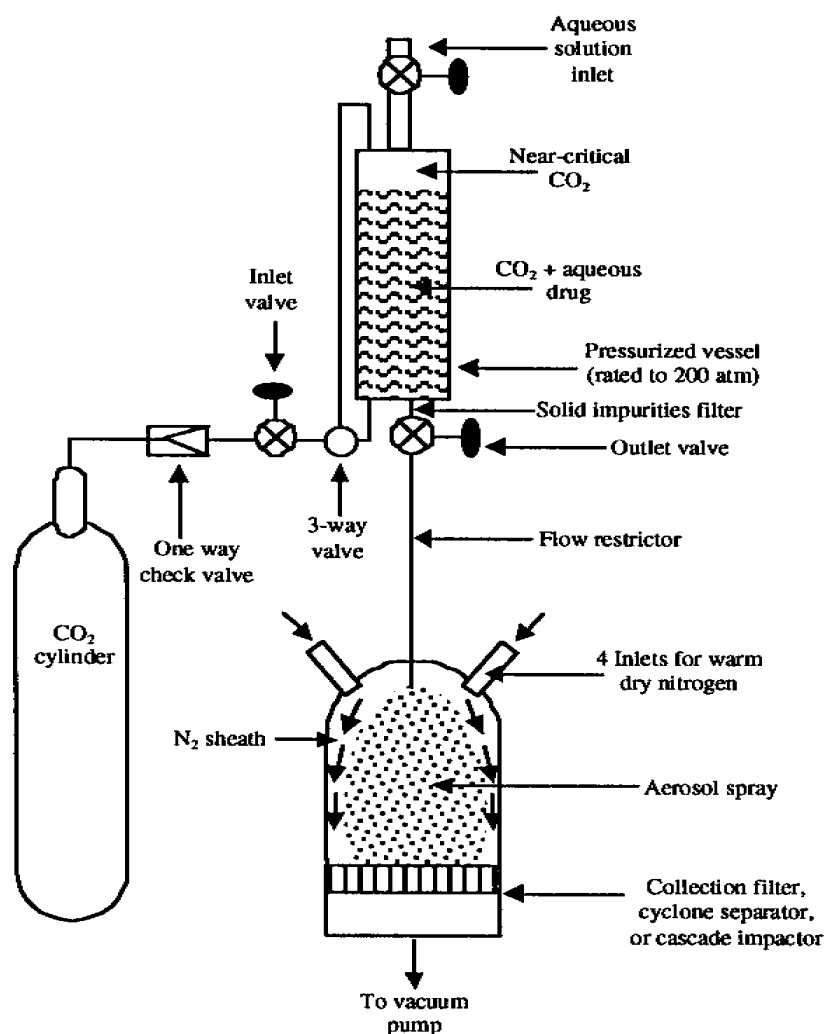
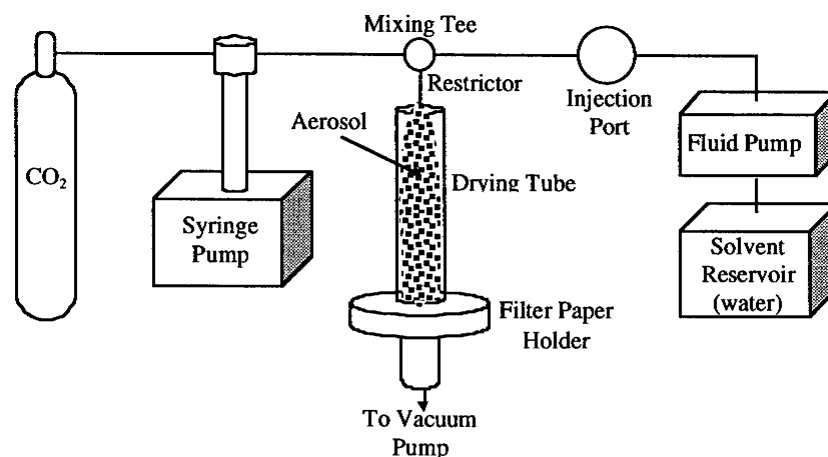
This paper describes new supercritical fluid technology that enables the formation of fine particles of a wide range of *water-soluble* substances^{1,2} by capitalizing on the relatively high solubility of supercritical or near-critical carbon dioxide in water (1-2% at normal operating conditions of room temperature and pressures around 100 atm). The dried particles produced typically have diameters in the 0.5 - 5 μm range, which make them useful for pulmonary drug delivery and various materials synthesis applications. Supercritical CO₂ offers the benefits of mild processing conditions (critical temperature and pressure of 31°C and 73.8 atm, respectively), low toxicity and lower cost (relative to organic solvents). In principle, the gas can be collected after the aerosolization process, purified, and condensed for reuse, although the technology does not produce CO₂ and utilizes gas produced in other processes.

METHOD AND RESULTS

Fine particle formation with supercritical CO₂-assisted aerosolization of aqueous solutions can be achieved using two methods. The first method utilizes the dynamic system (Figure 1), which produces a continuous delivery of aerosol through the simultaneous use of two pumps. The substance to be aerosolized is first dissolved in water at the desired concentration. This solution can consist of a single pharmaceutical or other material, or could be a combination of drug, excipient, and surfactant in varying ratios. The aqueous solution is then delivered to a low-dead-volume (< 1 μL) tee at a rate of 0.3-0.6 ml/min using an HPLC pump, where it is mixed with a stream of near-critical or supercritical CO₂ which has been pressurized to ~ 1500 psi. The resulting emulsion is expanded through a fused silica, stainless steel or PEEK restrictor (with an inner diameter ranging in size from 25 μm to several hundred microns) to produce a fine, dense aerosol plume. The aerosol can be passed into a glass tube through which warm nitrogen gas is flowed to enable drying of the aqueous droplets. If a glass drying chamber is used, drying can also be assisted by the use of an IR lamp external to the glass tube. Drying is achieved at a nitrogen flow rate of ~ 10 L/min and an inlet temperature of 70 °C using a glass tube that is ~ 1 inch in diameter and 7 - 8 inches in length. The warm gas is introduced using four inlets spaced evenly around the top of the tube. This creates a sheath of drying gas that prohibits the aqueous droplets from depositing on the walls of the tube

and carries them toward a filter paper collection system at the exit of the drying chamber. The dry powder is collected on cellulose acetate filter paper and is analyzed for particle size distribution and water content (using Karl Fischer titration) and/or stored in a humidity-controlled environment for later reformulation or delivery using a dry powder inhaler.

Figure 1. Schematic of dynamic supercritical CO₂-assisted aerosolization and bubble drying system.



The second method employs a canister into which the aqueous solution is placed and subsequently pressurized with liquid CO₂ at room temperature. This apparatus is referred to as the static system (Figure 2) and represents batch processing of the material to be aerosolized. After the system has been pressurized, the mixture is allowed to equilibrate to ensure that sufficient CO₂ has been dissolved in the aqueous solution. An exit valve at the bottom of the canister is then opened, and the aqueous solution (containing the drug and dissolved CO₂) is allowed to exit through a restrictor to create an aerosol plume. The aqueous droplets can then be dried as described for the dynamic system.

Both methods have been used to produce particles of various materials, including pharmaceuticals that are useful for treating lung-related illnesses, such as albuterol sulfate for the treatment of asthma and tobramycin sulfate for the treatment of bacterial infections in cystic fibrosis patients, and aerosols of rhDNase, a protein enzyme. Initial studies indicate that the technique is useful for

Figure 2. Schematic of static supercritical CO₂-assisted aerosolization system.

producing stable protein formulations due to the mild processing conditions and low drying temperatures. The latter is achieved through efficient aerosolization that is enhanced due to the expansion of the CO₂ dissolved in the aqueous solution, leading to further breakup of the aqueous droplets after the solution leaves the nozzle. This lower drying temperature reduces the stress experienced by proteins during other micronization process and allows for production of fine protein powders in the presence of stabilizing sugars and surfactants. The effects of stresses unique to the system (such as low pH due to the solubility of CO₂ in water) on protein stability are currently being investigated, and mitigated by adding buffers and other stabilizers.

For most materials, amorphous and spherical particles are produced that have diameters in the 0.5 - 5 μm range, as observed by scanning electron microscopy (SEM). Particle morphology is material dependent, as observed by scanning electron microscopy of particles produced from the aerosolization of a sodium chloride solution (Figure 3). In bubble drying NaCl, clusters of crystalline particles are observed. For tobramycin sulfate, spraying a solution containing only the drug leads to particles that are spherical, but with indentations or dimples (Figure 4), indicating that the particles may have partially collapsed during the drying process. Addition of a small amount of the drug (1%) to a lactose matrix returns the spherical morphology to the dried particles, with the tobramycin apparently assuming the morphology of the lactose, which is spherical, solid, and amorphous. It may be possible that some materials are hollow when aerosolized, as was observed using transmission electron microscopy on a mannitol particle that was produced using the technique. Investigations are underway to understand the effect of changing system parameters and surfactant identity and concentration on particle size and morphology for the wide range of materials that can be aerosolized with this technique.

SUMMARY

Supercritical CO_2 -assisted aerosolization is an effective method for the production of fine particles of water-soluble materials. The technology relies upon environmentally benign substances (carbon dioxide and water) to produce particles with diameters in the 0.5 - 5 μm range, potentially replacing conventional methods of particle micronization requiring organic solvents. The aerosolization process is efficient, enabling low temperature drying and making the technique well suited for heat-sensitive materials.

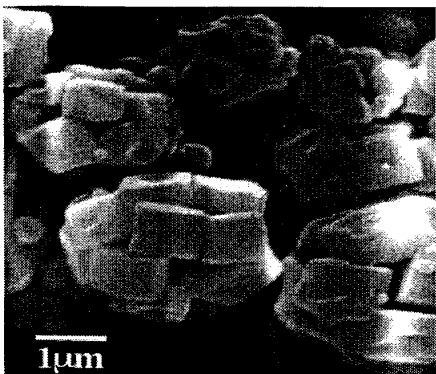


Figure 3. Scanning electron micrograph of NaCl aerosolized using supercritical CO_2 -assisted aerosolization system

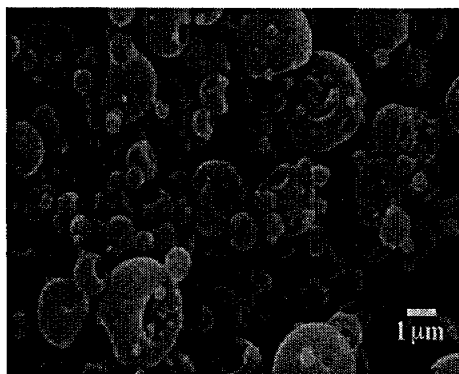


Figure 4. Scanning electron micrograph of tobramycin sulfate aerosolized using supercritical CO_2 -assisted aerosolization system.

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REFERENCES

1. R.E. Sievers, U. Karst, US Patent 5,639,441 (June 17, 1997).
2. R.E. Sievers, U. Karst, P.D. Milewski, S.P. Sellers, B.A. Miles, J.D. Schaefer, C.R. Stoldt, and C.Y. Xu, *Aerosol Science and Technology*, 30:3-15(1999).

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COATING APPLICATIONS WITH NEAR-CRITICAL CARBON DIOXIDE

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A Wurster-type coater employing $scCO_2$ as the fluidizing medium and antisolvent is described. Coating with $scCO_2$ allows the use of traditional organic soluble coatings with complete solvent recovery and virtually no atmospheric emissions. Glass inner and outer columns are housed in a high-pressure chamber in which $scCO_2$ is used to fluidize the substrates. The $scCO_2$ also removes the solvent from the coating solution sprayed on the substrates, thereby precipitating the coating. The system was used to coat a variety of substrates including glass, non-pareil and microcrystalline cellulose beads ranging in diameter from 0.3 to 2 mm, and tablets up to 5/16 inch. Examples from two general application areas will be presented. The first involves applying thin coatings on drugs for aesthetic/handling purposes or for delayed release applications such as taste masking. The second involves depositing drug microparticles on core substrates for fast-release applications. This process expands the range of substrate/coating combinations possible with the Wurster coater, making it feasible to coat water-soluble substrates with solutes sprayed from organic solutions.

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**DESIGNING SAFER
CHEMICALS AND MATERIALS**

A COMPUTATIONAL MODEL FOR DESIGNING SAFER CHEMICALS

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^{*}Department of Chemistry, Washington State University, Pullman, WA 99164**Abstract**

Cytochrome P450s are a superfamily of hemoprotein enzymes that perform chemical reactions through reduction of molecular oxygen. Found in all prokaryotes and eukaryotes, cytochrome P450s are varied in size, substrate specificity, and functionality while sharing a conserved mechanism, the catalytic cycle. These enzymes are primarily monooxygenases but can also perform many other types of reactions. In almost all organisms, P450s serve multiple roles. First, they metabolize reactions in the biosynthesis of steroids, fatty acids, and antibiotics. Second, they metabolize exogenous substrates such as drugs, chemicals, and environmental contaminants in detoxification reactions.

Sometimes, P450s metabolize less toxic substrates into more toxic products, a process called bioactivation. Years of study have shown that the toxicity for many compounds is due to their metabolites and not to the parent compound. Of the many P450 mediated mechanisms that cause bioactivation, the best known is via hydrogen atom abstraction. Because the toxicity of many compounds is dependent on the rate of hydrogen abstraction, the structure of these compounds may be correlated with toxicity. This shared mechanism provides a way to quantitatively estimate the rate of bioactivation, allowing a method of classifying similar compounds according to their toxicity. By developing a model based on this mechanistic knowledge, predictions can be made for new chemicals or chemicals that lack toxicological data.

One way to make a predictive model is through computational techniques. This is made possible by the fact that the calculation need only contain the substrate and a model for the heme. Also, the conserved reaction mechanism makes the model applicable for all isoforms. Three criteria were established to guide model development: 1) the model must contain an oxygen that mimics the reactive oxygen species in the catalytic cycle; 2) a linear free energy relationship must exist, so the rates of hydrogen atom abstraction can be predicted based on ground state properties alone; and 3) the model must reproduce known experimental results. The para-nitrosophenoxy radical (PNR) best mimicked the reactive oxygen species based upon semiempirical calculations (Jones, 1996). The second criteria was established because transition state calculations can be tedious. This led to a search of parameters that would correlate activation energies while providing rapid results. The use of the ionization potential (IP) of the intermediate carbon radical and the heat of reaction resulted in a good correlation ($r^2 = 0.94$) (Korzekwa *et al.*, 1990). The third criterion was evaluated by examining the bioactivation of two classes of compounds: nitriles and halogenated hydrocarbons.

Nitriles are cyano (CN⁻) containing compounds that are important in the manufacture of pharmaceuticals, polymers, plastics, vitamins, fibers, and solvents. These many uses make nitriles an attractive target for safe design. The toxicity of nitriles is based upon the ability of P450s to abstract a hydrogen from the alpha carbon, causing the release of cyanide (**Figure 1**). A previous study correlated the acute toxicity (LD₅₀) of 26 nitriles with their water - octanol partition coefficient (log P), resulting in poor correlation ($r^2 = 0.35$) (DeVito and Pearlman, 1991). Using the PNR model along with log P and an additional descriptor (k_{corr}), a factor that represents the rate of hydrogen abstraction at the alpha carbon based upon the nitrile structure, a better correlation was obtained ($r^2 = 0.72$) (Grogan *et al.*, 1992). Thus, this model can be used as a tool to estimate the toxicities of nitriles under consideration for synthesis and development.

Halogenated hydrocarbons are also commercially important substances used in refrigerants, solvents, and inhalation anesthetics. Halogenated hydrocarbons that contain a hydrogen atom and two halogen atoms on a terminal carbon can undergo P450 metabolism, yielding acid halide metabolites (**Figure 2**). These metabolites are electrophilic, and are responsible for a variety of toxic effects (Anders, 1985). The bioactivation mechanism involves hydrogen abstraction from the terminal carbon and the toxicity is a function of the rate of acid halide formation. Therefore, a way to develop safer halogenated hydrocarbons would be to design one that will not be readily metabolized to acid halides.

Again, the PNR model was used to predict the rate of hydrogen atom abstraction from six halogenated hydrocarbons. The activation energy of carbon radical formation was calculated and compared to *in vitro* rates of

trihaloacetic acid formation in expressed human 2E1 microsomes, an isoform shown to be primarily responsible for small haloalkane metabolism in the human liver (Yin *et al.*, 1995). The resulting correlation was excellent ($r^2 = 0.97$). The model was also used to examine fluoride ion formation, which is believed to cause kidney damage at high exposures, such as in inhalation anesthetics. This correlation was also good ($r^2 = 0.86$).

There are also some disadvantages to using the PNR model. The model predicts only electronic components of P450 hydrogen atom abstraction and does not take into account the steric factors involved in substrate-active site interactions. Also, the model fails to consider pharmacokinetics and enzyme kinetics, which is important when the oxidation step is fast relative to the other steps in the pathway. Finally, the model will fail if the toxicity does not arise from the chosen bioactivation pathway.

Another approach to designing safer chemicals is through the use of stereoselective biocatalysts. Biocatalysis is the production of commercially important chemicals through enzyme catalysis. Our hypothesis is that Cytochrome P450s have the potential to be biocatalysts, specifically in oxidation reactions, where current industrial methods are problematic.

Industrial oxidation reactions are problematic for several reasons. Cytochrome P450 mediated oxygenation reactions may be able to resolve these problems. We have chosen to examine a specific reaction, the production of 2-ethylhexanoic acid from 2-ethylhexanol (**Figure 3**). 2-Ethylhexanoic acid is a medium chain carboxylic acid with many commercial applications. It has one of the highest production rates of carboxylic acids. Because it contains a stereogenic center, 2-ethylhexanoic acid has 2 enantiomers. Industrial synthesis produces a racemic mixture containing equal amounts of R and S.

Human exposure occurs through its synthesis and handling or through exposure to products that contain it. One of the main routes of exposure is by di(2-ethylhexyl) phthalate (DEHP) ingestion from foodstuff plastic containers that leach this compound. Another way is by blood transfusions that use plastic bags. Mammalian studies have shown 2-ethylhexanoic acid is the primarily metabolite of DEHP. While 2-ethylhexanoic acid is not acutely toxic, several animal studies indicate that the R enantiomer is a potent teratogen while the S enantiomer is not. On this premise, we hope to design P450s to perform stereospecific oxidation of 2-ethylhexanol to 2-ethylhexanoic acid, thus making a safer chemical.

References

- Jones, J.P. (1996) *Designing Safer Chemicals*, pp. 116-137, American Chemical Society.
 Korzekwa, K.R.; Jones, J.P.; Gillette, J.R. *J. Am. Chem. Soc.* 1990, 112, pp. 7042-7046.
 DeVito, S.C.; Pearlman, R.S. *Med. Chem. Res.* 1991, 1, pp. 461-465.
 Grogan, J.; DeVito, S.C.; Pearlman, R.S.; Korzekwa, K.R. *Chem. Res. Toxicol.* 1992, 5, pp. 548-552.
Bioactivation of Foreign Compounds; Anders, M.W., Ed.; Academic Press:New York, 1985.
 Yin, H.; Anders, M.W.; Korzekwa, K.R.; Higgins, L.; Thummel, K.E.; Kharasch, E.D.; Jones, J.P. *Proc. Natl. Acad. Sci. USA* 1995, 92, pp. 11076-11080.

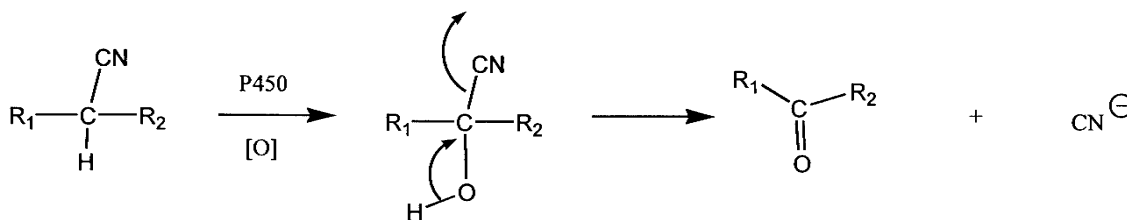


Figure 1. Proposed mechanism of nitrile toxicity.

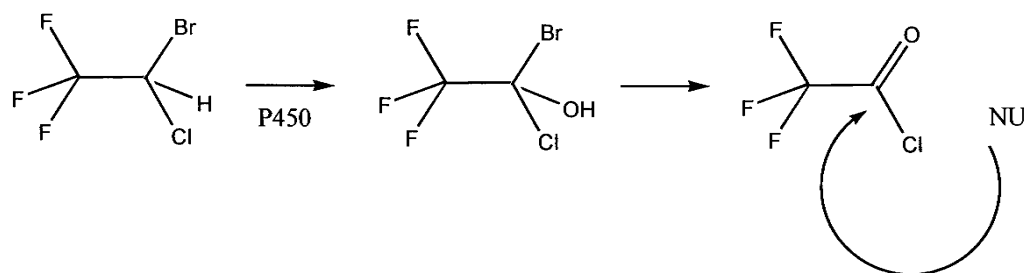
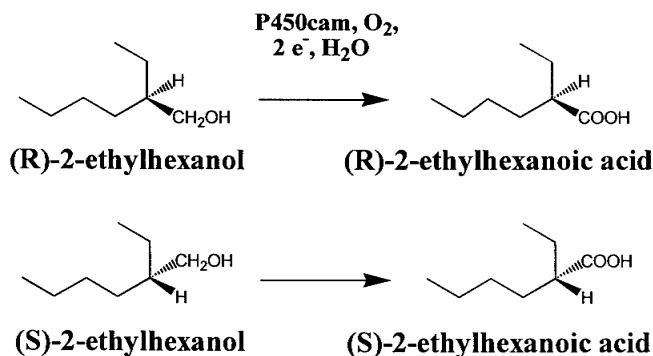


Figure 2. Proposed mechanism of hydrochlorofluorocarbon (HCFC) toxicity. NU= Endogenous nucleophile



A NEW ENVIRONMENTALLY SENSIBLE CHLORINE ALTERNATIVE

William F. McCoy

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ABSTRACT

Industrial water treatment is necessary for energy conservation and to ensure a sustainable global supply of freshwater. Far more chlorine is used to control microbial fouling in industrial water compared to any other chemical. An environmentally sensible chlorine alternative is needed because handling the gas is hazardous, the liquid is not stable, combined residuals are not effective, free residuals do not control biofilms, and disinfection byproducts are toxic. For industrial water treatment, these problems have now been largely overcome with a novel (the first) and unique (the only) stabilized liquid bromine antimicrobial. Although other stabilized halogen antimicrobials are well known in water treatment, none have substantially overcome the fundamental application problems of chlorine and bromine in industrial water treatment. This new product is the first biomimetic industrial antimicrobial, having been designed to imitate the Stabilized bromine antimicrobials produced in mammalian immune systems. The new antimicrobial is modeled after the N-bromoamidoalkylsulfonates produced by eosinophils during the respiratory burst. It is an order of magnitude less toxic, several orders of magnitude less volatile, easier to handle, more compatible with other water treatment chemicals, more effective against biofilms, and it generates less than half the disinfection by-products compared to chlorine or other alternatives. One hundred fifty billion gallons of industrial water have by now been successfully treated globally. Use of this new antimicrobial has substantially reduced environmental and human health risks from industrial water treatment by replacing from field use nearly thirty million pounds of chlorine. The new product is proven to comparatively perform better, more safely, and it is substantially easier to apply than chlorine. It is widely held that this innovation and its commercial development resulted in a technological breakthrough that has established a new class of stabilized bromine antimicrobials.

INTRODUCTION

Since 1996, more than two thousand water treatment field engineers from every industrialized country and from many developing countries on every continent (except Antarctica) have been uniquely trained in microbial fouling

control based upon sound principles in environmental microbiology. The foundation for technical and commercial success in this original approach is the industrial imitation of microbial fouling control strategies observed in nature. Field practice is arranged into three categories of key principles in natural microbial fouling control: Recognition, Remedy, and Regulation. Recognition refers to the discovery of microbial fouling problems and then, determination of the value to be derived from solving root-causes of these problems. This requires use of modern diagnostic techniques in microbiology and an understanding of the science since, for example, root-causes are so often associated with complex microbial communities on surfaces. Remedy refers to actions taken to minimize or eliminate root-causes of microbial fouling problems. This requires focus of the goal onto managing the overall microbial fouling process. Attempting to simply treat symptoms of the problem, such as has often been done in the past, is shown to be economically unacceptable. Regulation refers to proactive variance of the applied remedy so that the stresses applied will effectively control, for example, the complex surface fouling communities of microorganisms so often found to be at the root-cause of important industrial water treatment problems. Complex communities of microorganisms adapt frankly and quickly to the environmental stresses caused by applied industrial antimicrobials. Environmentally sensible strategies to manage the root cause of industrial microbial fouling problems must involve varying such stresses proactively and intelligently. This practical approach to industrial water treatment has been readily accepted because of its compelling feasibility, its basis in environmentally sound principle, and because the marketplace value of success is tangible.

SUMMARY

The new industrial chlorine alternative was purposefully designed to imitate the stabilized bromine antimicrobials produced naturally in the human immune system. It is the first biomimetic industrial biocide. It is chemically analogous to the antimicrobial product of the oxidative respiratory burst in eosinophils, a type of mammalian white blood cell. These cells consume oxygen in a cellular process recently proven to produce Stabilized bromine antimicrobials.^{1,2} In eosinophils, HOBr from the enzymatically-catalyzed oxidation of bromide with H₂O₂ immediately reacts with 2-aminoethanesulfonic acid (taurine). The product of this stabilization reaction is a potent antimicrobial, N-bromoaminoethanesulfonic acid and it is the design model for the new industrial antimicrobial. Amidosulfonic acid (sulfamic acid) is used to stabilize bromine in the patented proprietary process to manufacture and to use the new product. Sulfamic acid is the reaction product of ammonia and chlorosulfonic acid, or it can be obtained by heating urea and sulfuric acid. It has been used in industrial water treatment for many years as a cleaning agent and as a means to protect organic water treatment chemicals from the oxidative effect of halogens. It is generally recognized as safe (GRAS) in CFR21 186.1093 for use as an indirect food ingredient.

In aquatic habitats, natural bromine antimicrobials are also preferred microbial fouling control agents. Certain red and brown seaweed, such as the brown alga *Ascophyllum nodosum*, selectively oxidize bromide in the ocean and are known to produce substantial quantities of HOBr directly upon their surfaces³. This process is analogous to the oxidative burst that occurs in mammalian white blood cells. Natural control of microbial fouling is the means by which seaweed avoid the kind of biofouling that rapidly occurs, for example, on the surfaces of ships and piers. Bromine antimicrobials are superior in alkaline pH (seawater is always above pH 8), in the presence of nitrogenous organic matter, and due to lower volatility.^{4,5} The pKa acid dissociation constants for HOCl and HOBr are 7.4 and 8.8, respectively; the dissociated acids are not effective antimicrobials. Table 1 shows the effect of acid dissociation on antimicrobial performance in well-controlled laboratory experiments.

Table 1. The effect of acid dissociation on antimicrobial performance against *Pseudomonas aeruginosa* at equivalent oxidant concentrations and contact times

Chlorine			Bromine		
pH	% HOCl Acid	Log (bacteria killed/ml)	pH	% HOBr Acid	Log (bacteria killed/ml)
7.0	79	5.8	7.0	99	5.9
7.5	50	4.8	7.5	98	5.9
8.0	30	3.5	8.0	90	5.9
8.5	12	<1	8.5	65	5.8
9.0	4	<1	9.0	40	4.0

This data shows that bromine works better than chlorine in high pH waters, such as the ocean. Similarly, most industrial water is quite alkaline and therefore, a practical form of bromine is also preferred. The new stabilized bromine antimicrobial⁶ is an excellent antimicrobial having been proven superior in field and laboratory

experiments compared to chlorine, stabilized chlorine, and equal to or better than solid hypobromite antimicrobials. The product is effective for the control of microbial biofilms and highly diverse microbial communities, including those that harbor *Legionella*.⁷

STABREX® Stabilized Liquid Bromine is far more stable than liquid chlorine bleach. Table 2 shows of the stability of the new product compared to industrial strength chlorine bleach.

Table 2. Storage stability of chlorine and stabilized liquid bromine

% Oxidant Remaining at 77°F Continuously			% Oxidant Remaining at 131 °F Continuously		
Storage Days	Industrial Bleach	STABREX	Storage Days	Industrial Bleach	STABREX
0	100.0	100.0	0	100.0	100.0
12	90.2	98.3	1	76.8	96.6
32	83.9	98.3	3	40.2	96.6
135	59.2	97.4	7	26.8	86.2
246	43.4	96.4	12	16.1	75.9
600	23.5	95.2	20	8.9	65.5
800	18.7	94.0	33	5.4	53.4

Several tons of product were shipped to India and stored for one year above 90 °F. The product was within specification (less than 10% degraded) for the entire year, after which it was used to control fouling in an industrial water system. Chlorine would have been completely degraded in this time under these conditions. Chemical wastage was eliminated. Accident risk in transporting oxidant was reduced because less volume was necessary.

Hypobromite solutions are even more unstable than hypochlorite. Hypobromite disproportionates to bromate, a toxic and potentially carcinogenic compound. The stabilizer in STABREX inhibits that process.

Table 3. Stability to bromate formation

Oxidant (Equivalent Concentrations)	% Bromate After 60 Days Storage	Volatility is the principle technical problem with many chlorine alternatives because most industrial systems are
Sodium Hypobromite	2.7	
Stabilized Liquid Bromine	0.004	

open to the atmosphere and the treated water is vigorously recirculated. The volatility of STABREX is lower than any other oxidizer used for industrial water treatment.

Table 4. Relative volatility of oxidizing chemicals

Oxidizing Chemical	Air-Water Partition Coefficient (Atm @ 20°C)	Relative Volatility (Normalized)
Ozone	5,000	125,000
Chlorine (elemental)	585	15,000
Bromine (elemental)	59	1475
Chlorine Dioxide	54	1350
Hypochlorous Acid	0.08	2
Hypobromous Acid	0.04	1
STABREX	<<0.04 ^a	<<1

^aVolatility was below the limit of measurement in the method used

Chlorine is highly reactive with scale and corrosion inhibitors. These reactions are counter-productive. STABREX is less aggressive to many inhibitors such as those indicated in Table 5.

Lower chemical reactivity with non-target molecules is useful for another performance-related reason. Compared to unstabilized chlorine or bromine, STABREX more effectively penetrates and disinfects biofilms (the adherent microbial communities that cause detrimental surface-fouling effects in water cooling systems). Microorganisms prefer the protection and luxuriant environment in biofilms. Most of the viable microorganisms in industrial systems are found in biofilms, not floating around freely in the bulk recirculating water.

Table 5. STABREX is more compatible with water treatment compounds

Oxidizing Chemicals ^a	AMP ^b % Reverted \pm std dev	TT ^c % Degraded \pm std dev
None	0.9 \pm 1.3	0 (normalized)
Chlorine	39.0 \pm 2.8	18.1 \pm 0.1
Bromine	20.7 \pm 1.3	96.6 \pm 1.3
STABREX	4.1 \pm 1.9	2.2 \pm 4.6

^a5 ppm total residual oxidant (measured) for 1 hr. Contact^bAMP is aminotrimethylene phosphonic acid and is useful as a scale inhibitor^cTT is tolyltriazole and is useful as a yellow metal corrosion inhibitor**Table 6.** Performance of equivalent treatments of bromine antimicrobials against biofilms

Oxidizing Chemical	% Removal of Biomass (\pm std dev)	% Decrease in Fluid Frictional Resistance (\pm std dev)	Biofilm Disinfection (Log Reduction in Viable Bacteria/cm ²)
Unstabilized Bromine	2 \pm 2	3 \pm 3	3.4 \pm 0.2
STABREX	45 \pm 2	47 \pm 18	5.2 \pm 0.2

STABREX is safer because it is less toxic to aquatic wildlife (Table 7) and because less chemical is required to control microbial fouling.

Table 7. Toxicity of STABREX Microorganism Control Chemical compared to unstabilized bromine

Aquatic Toxic Test (LC ₅₀) ^a	Unstabilized Bromine (ppm as Br ₂)	STABREX (ppm as Br ₂)	Reduction in Toxicity
Rainbow Trout (96h LC ₅₀)	0.23	0.60	2.6 x
<i>Daphnia magna</i> (48h LC ₅₀)	0.04	0.58	14.5 x
Sheepshead Minnow (96h LC ₅₀)	0.19	2.30	12.1 x
Mysid Shrimp (96h LC ₅₀)	0.17	3.65	21.5 x

^aLC₅₀ is the lethal concentration for 50% of the test organism after 96h or 48h contact

Disinfection by-products (e.g., adsorbable organic halides such as trihalomethanes) are more than 50% decreased compared to equivalent chlorine treatments in standardized AOX test with STABREX⁸. In practice, disinfection byproducts are decreased even further in STABREX applications because less oxidant is required to control the microbial fouling process compared to bromine or chlorine applications.

STABREX is easier and simpler to use compared to any other oxidant available for industrial water treatment. The product is pumped directly from returnable transporters (PortaFeed[®] Systems)⁹ with standard chemical feed equipment. Previously, the only practical ways to apply bromine were to oxidize bromide solutions on-site with chlorine gas or chlorine bleach in dual liquid feed systems, or with one of the solid organically-stabilized bromine products applied from sidestream erosion feeders. The former is cumbersome and complex, and the latter is prone to dusting and difficult to control. Other oxidants require complex handling and feed of toxic volatile gases, unstable liquids, multiple-component products, or reactive solids. Simplicity in use results in reduced risk to workers and to the environment.

The benefits of replacing chlorine with STABREX are in reducing environmental toxicity (because it is less toxic to aquatic wildlife), in reducing accident risk (because it is less hazardous and easier to handle), and in reducing chemical waste (because it works better, is more stable in transport/storage, is less volatile and less reactive). Environmental toxicity and accident risk have been substantially reduced in more than 2,000 industrial water systems worldwide.

Significant industrial demand for a more practical stabilized liquid bromine product has been known for several years. Until the invention and commercial development of STABREX, there was no practical means to overcome the inherent instability, volatility, and handling hazards of liquid bromine. The new technology solves several long-standing technical problems that bromine manufacturers tried, unsuccessfully, to overcome for 15 years. The practical use of STABREX stabilized liquid bromine and its successful application in microbial fouling control is new to the industrial world of water treatment.

1. Science. 1986. 234:200-203
2. Journal of Biological Chemistry. 1995. 270(7):2906-2913.
3. Environmental Science and Technology. 1991. 25:446-449.
4. Water Research. 1992. 26:99-102
5. Cooling Tower Institute, Paper No. TP90-09. Houston, TX (281) 583-4087 www.cti.org
6. STABREX® Stabilized Liquid Bromine is a trademark of Nalco Chemical Company
7. National Association of Corrosion Engineers International. 1997. CORROSION '97 Paper No. 398. P.O. Box 218340, Houston, Texas 77218.
8. U.S. Patent #5,683,654.
9. PortaFeed® is a registered trademark of Nalco Chemical Company, Naperville, IL

A NEW ENVIRONMENTALLY PREFERRED COPPER CORROSION INHIBITOR

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ABSTRACT

Copper alloys are widely used in industrial cooling water systems. However, a copper corrosion inhibitor is needed to prevent equipment failures and to reduce the discharge of extremely toxic copper compounds into the environment. Although azoles such as benzotriazole and tolyltriazole have been used to protect copper alloys, they react with oxidizing halogens that are commonly used to control microbiological activity. The reaction of these azoles with chlorine, for example, produces species that are not protective to copper. In systems with mixed metals, dissolved copper from corrosion also leads to higher corrosion rates of mild steel. New halogen resistant azole (HRA) technology has been developed that does not react with halogens and protects copper in cooling systems that are being halogenated. This inhibitor significantly reduces copper and steel corrosion and resulting equipment failures, decreases chlorine usage and copper discharge, and reduces the overall use and discharge of treatment chemicals into the environment.

INTRODUCTION

Copper alloys have excellent heat transfer properties and are extensively employed in cooling systems. Azoles are commonly used to protect these alloys from corrosion^{1,2}. These chemicals are very effective corrosion inhibitors and, under many cooling water conditions, provide excellent copper protection at dosages of as little as 1 to 3 mg/L. Tolyltriazole (TTA) is by far the most extensively used azole^{3,4}.

While the use of azoles for corrosion inhibition is widespread, they do have drawbacks. The most important drawbacks are experienced when azoles are used in combination with oxidizing halogens, which are used to control microbiological growth in cooling water systems. When copper alloys that have previously been protected with azoles are exposed to an oxidizing halogen, corrosion protection breaks down. After breakdown, it is difficult to form new protective films in cooling systems that are being halogenated. TTA-treated systems that are chlorinated are particularly susceptible to this loss of copper protection. Chlorine reacts with TTA in cooling systems and drastically reduces its effectiveness as a copper inhibitor. When chlorine is applied to a TTA-treated system, a caramel-like odor is observed that is characteristic of the TTA decomposition product formed in the cooling water⁵. Concurrent with the application of chlorine and the decomposition of TTA, increases in copper corrosion rates are observed. This is often accompanied by severe mild steel corrosion in the form of pitting, caused by the increased concentration of dissolved copper and the resulting galvanic effect between copper and steel. When corrosion protection is lost, TTA feedrates in the cooling water are usually increased in an attempt to overcome the reaction with chlorine and maintain a high enough residual to protect the copper surface. Very high dosages of tolyltriazole are frequently applied in order to improve performance, often with limited success.

Several azole derivatives are discussed in this paper. Laboratory results show that modification of azole molecules significantly affects the susceptibility of the inhibition film to chlorine attack. A number of compounds show superior copper corrosion inhibition over tolyltriazole and benzotriazole. In particular, new halogen resistant azole (HRA) technology⁶⁻⁹ has demonstrated excellent performance in the laboratory and in the field.

RESULTS

Laboratory tests were conducted in a Beaker Corrosion Test Apparatus, which consisted of a 2 liter beaker equipped with an air/carbon dioxide sparge, a magnetic stirrer, and a corrosion monitoring system. Figure 1 shows copper corrosion in a 500 ppm Ca (as CaCO₃) water at pH 7.2 and 120 °F. Copper probes were immersed in the test water with or without 3 mg/L of an azole compound for about 18 hours. As the corrosion rate stabilized, 5 mg/L sodium hypochlorite (as free chlorine) was introduced and the tests were continued for another 22 hours.

During the first 18 hours, the copper corrosion rate remained relatively high without any azole inhibitor (Blank). On the other hand, solutions containing TTA and HRA showed excellent copper corrosion control. Instant and dramatic increases in corrosion rate were observed in the blank and TTA solutions after the chlorine addition. This is indicative of inhibitor film breakdown. The corrosion rate for the blank increased to 18 mpy in 1 hour. The corrosion rate for TTA reached 2.5 mpy in about 3 hours after hypochlorite feed and remained nearly unchanged afterwards. In contrast, the corrosion rate for HRA remained very low (0.03 mpy). Area under the curve calculations for the three solutions indicated that the copper release would be 0.62 mg/L for the blank, 0.34 mg/L for the TTA solution, and 0.0062 mg/L for the HRA solution.

A field comparison of TTA with HRA was made at a southeastern nuclear power plant. The cooling system at the plant has a volume of 7,000,000 gallons and a blowdown (discharge) rate of 2,600 gal/min. Their heat exchanger equipment is primarily 90:10 copper/nickel and has a surface area of 600,000 ft². The plant shot feeds a sodium hypochlorite solution to the cooling water twice per day to control microbiological activity.

The trial began with TTA being fed at 3.0 mg/L for a 2 week baseline period. Following this, HRA was fed at 2.0 mg/L for 2 weeks. During the 1 month period, corrosion rates were monitored continuously using a linear polarization technique. The Cu:Ni alloy corrosion rates for the trial are presented in Figure 2. Each peak on the graph represents the Cu:Ni corrosion rate during the hypochlorite feed. As the figure shows, there was a dramatic decrease in corrosion rates when HRA was fed. Particularly striking was the 60% to 80% reduction in the corrosion rate spikes during chlorination.

SUMMARY

New halogen resistant azole (HRA) technology has been developed for copper corrosion protection in aqueous solution. The new material forms more tenacious protective films on the copper surface, providing superior corrosion protection for both copper alloys and low carbon steel in the presence of halogen-based oxidizing biocides. This novel material has numerous environmental benefits as summarized below:

1. HRA is stable in the bulk water, giving a better-controlled residual level, which ensures corrosion protection with lower treatment levels. Better copper protection reduces the release of copper into the water. Replacing TTA with HRA produces a positive environmental effect, as measured by actual toxicity studies at a field site.
2. The reactivity of HRA with halogens is minimal, eliminating the odor and reducing the system demand for halogens.
3. HRA not only reduces copper corrosion but also significantly reduces copper induced pitting on low carbon steel. This results in extended equipment life, particularly in mixed metal systems.
4. The application of HRA reduces the overall use and discharge of treatment chemicals into the environment.

REFERENCES

1. Y. Lin, Y. Guan, K.N. Han, *Corrosion Science* **1995**, *51*, 367-375,
2. Z. Xu, S. Lau, P.W. Bohn, *Langmuir* **1993**, *9*, 993-1000.
3. O. Hollander, R.C. May, *Corrosion* **1985**, *41*, 39-45.
4. F. Lu, N.M. Rao, B. Yang, J.E. Hoots, R.S. Budry, *Corrosion* **1994**, *50*, 422-431.
5. T.C. Breske, *Materials Performance* **1983**, *22*, 48-52.
6. D.W. Reichgott, S.B. Anderson, M.A. Cady, R.C. May, A.G. Monino, US Patent # 5,772,919 **1998**.

7. S.B. Anderson, M.A. Cady, US Patent # 5,773,627 **1998**.
8. D.W. Reichgott, S.B. Anderson, M.A. Cady, R.C. May, A.G. Monino, US Patent # 5,863,463 **1999**.
9. D.W. Reichgott, S.B. Anderson, M.A. Cady, R.C. May, A.G. Monino, US Patent # 5,863,464 **1999**.

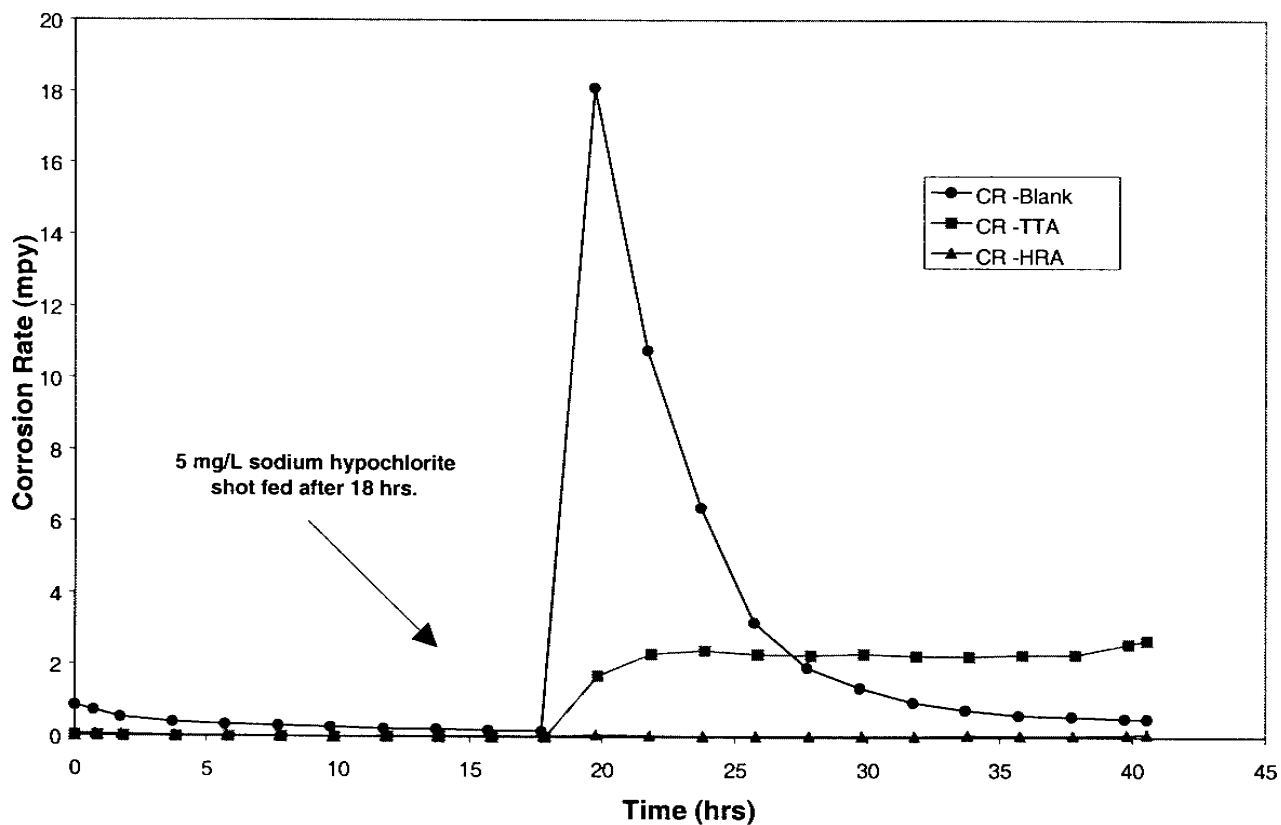


Figure 1. Beaker Corrosion Test for Copper at pH 7.2.

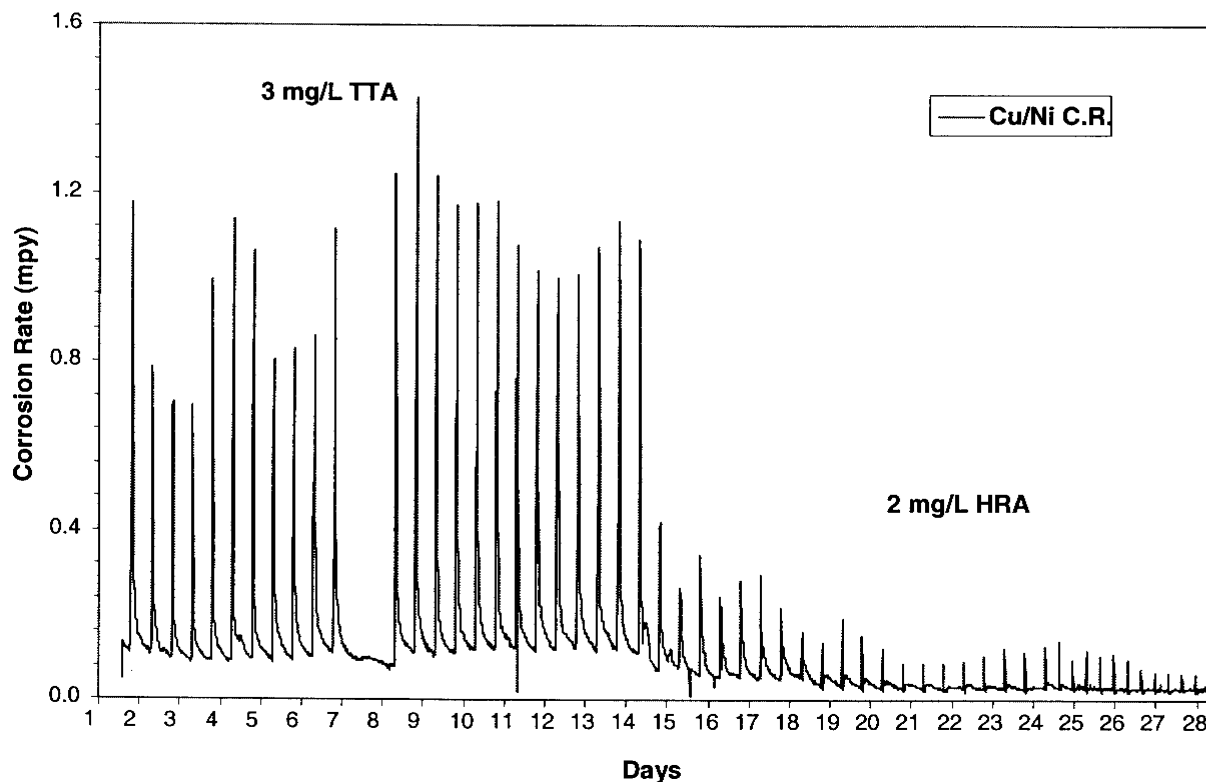


Figure 2. Cu:Ni Corrosion Rates (Southeast Nuclear Plant)

EFFICIENT, CLEAN, AND VERSATILE FISCHER-TROPSCH VEHICULAR FUELS

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ABSTRACT

Sustainable use of green chemistry in vehicular fuels often demands that the fuels be cost competitive, clean burning, capable of being produced from indigenous resources, and compatible with the existing vehicular fuel infrastructures. Furthermore, advocates of alternative fuels rarely present a unified approach that would allow different interests to increase their effectiveness. Recent developments in Fischer-Tropsch fuels may present a rare and valuable opportunity for a unified approach in this quest.

This paper reviews recent advances in direct utilization of unrefined Fischer-Tropsch liquids (FTL) as vehicular fuels. These advances include recent engine tests of FTL-ethanol mixtures exhibiting dramatic decreases in particulate emissions and slightly lower NO_x emissions than standard diesel. These fuels and our current fuel distribution infrastructure are compatible with production from natural gas, coal, biomass, and municipal solid waste—advocates for using each of these feedstocks could unify behind a common approach that could evolve with technology, resource availability, and incentives.

INTRODUCTION

Excluding tap water, liquid fuels are the largest volume commodity chemical used by the general public. As such, changes in product synthesis and utilization can have dramatic impacts on environmental impact, national security, and national/international economies.

Today's fuels are a result of decades of the parallel evolution of both the fuels and applications. As such, these fuels have detailed specifications and will not be easily displaced by green chemistry alternatives. It is likely that any strides toward greener fuels will have to be based on long term strategies that include environmental impact as one of many factors on which fuel selection is based.

Table 1 lists those fuel properties that have the greatest impact on fuel selection. Motivated by factors ranging from fuel cost to safety and environmental impact, each of these properties are important for the acceptance of a fuel. Table 2 presents a largely qualitative rating of each of these fuels based on the author's perceptions in today's market. Factors such as liquid fuels being preferred over gaseous fuels are considered since consumers prefer liquids. Pipeline distribution is considered because of the historic significance of distribution costs impacting the success or failure of major oil companies. High efficiency refers, ultimately, to the efficiency of which the energy at the raw material source is converted to energy at the vehicle's wheels. Diesel engines are rated higher in this category since diesel engines are typically about 30% more efficient than gasoline engines.

Table 1. Fuel properties that impact fuel selection and utilization.

Property	Preferred State	Reason
Ease of Handling	Liquid	Consumer Acceptance
Compatible with Existing Pipelines	Hydrocarbon	Cost
Low Incremental Vehicular Cost	No Changes	Cost
Resistance of Fuel to Fire (Safety)	Flash Point > 40 C	Safety
Long-Term Energy Security/Versatility	Domestic Production	Embargoes/Monopolies
Sustainability	Renewable, Biomass-Derived	Replacement Costs
High Efficiency	High Source to Wheel Efficiency	Cost & CO ₂ Emissions
Cost Competitive	Low Cost per BTU	Cost
Low Emissions	Low HC, NO _x , and PM	Environment

Table 2. Rating of typical fuels and alternatives based on Table 1 properties. Rating system is + (advantage), 0 (neither advantage nor disadvantage), and - (disadvantage). Score sums rate with a value of 1 for +, 0 for 0, and -1 for -.

	Gasoline	Diesel	Propane	Natural Gas	Ethanol	Methanol	Biodiesel	FT Diesel	FT Liquid	Simple Ethers	Complex Ethers
Ease of Handling	+	+	///	///	+	+	+	+	+	-	+
Compatible with Existing Pipelines	+	+	+	+	-	-	0	+	+	-	0
Low Incremental Vehicular Cost	+	+	-	-	0	0	+	+	+	-	+
Resistance of Fuel to Fire (Safety)	0	+	-	-	0	-	+	+	0	///	+
Long-Term Energy Security/Versatility	///	///	-	0	+	+	0	+	+	+	+
Sustainability (Large Volume)	+	+	+	+	+	+	///	+	+	+	+
High Efficiency	0	+	+	+	0	0	+	+	+	+	+
Cost Competitive	+	+	+	+	///	+	-	0	+	0	-
Low Emissions	+	0	+	+	+	+	0	+	+	+	+
Score	5	6	1	2	2	3	4	8	8	0	6

With the exception of methanol, Fischer-Tropsch diesel, Fischer-Tropsch liquids, and complex ethers, most of the fuels of Table 2 have major drawbacks that will likely put them at a disadvantage in the long run. For gasoline and diesel, these major drawbacks are the long term energy security associated with limited petroleum resources. For propane and natural gas, consumer acceptance of handling gaseous fuels presents a major obstacle. Ethanol and biodiesel have disadvantages associated with cost competitiveness even in the most optimistic scenarios. In addition, biodiesel simply cannot be produced in large enough quantities to have a significant impact on the fuel market. Simple ethers have safety-related problems due to their flammability.

Table 3 lists the key issues surrounding those four fuels that show the greatest potential for meeting long-term liquid fuel needs in the U.S. Data are available in the published literature on methanol and Fischer-Tropsch

diesel. On the other hand, little data are available on complex ethers—the subject is currently shrouded in industrial secrecy, and the fuels may not be cost competitive. The purpose of this paper is to summarize the properties and performance of Fischer-Tropsch liquids for which information is available but not well known.

Table 3. Fuel properties that impact fuel selection and utilization.

Fuel	Greatest Concerns
Methanol	Low flash point and high volatility are undesirable. Not compatible with existing fuel pipeline distribution.
Fischer-Tropsch Diesel	Refining and isomerization processes are needed and both increase costs and decrease conversion efficiencies.
Fischer-Tropsch Liquids	Use of C ₇ and C ₈ compounds decreases flash point to levels outside diesel fuel specifications.
Complex Ethers	Technology that allows economical product is either not available or at least not disclosed.

SUMMARY

Fischer-Tropsch liquids (FTL) are rather loosely defined as that portion of Fischer-Tropsch reaction product that is liquid at temperatures down to about 2°C. Historically, this is the fraction of product that is attained by the combination of vapor-liquid flash separations and mild hydrocracking of C₂₀₊ compounds to arrive at a liquid product that is suitable for pipeline or tanker transport to refineries. FTL may also be referred to as synthetic crude or white crude since it has historically been treated as a refinery feedstock, similar to crude oil. Both isomerization and distillation are used to convert FTL to conventional naphtha, kerosene, and diesel at the refinery.

Figure 1 illustrates the three-step process for Fischer-Tropsch conversion of raw materials (natural gas, coal, biomass, or trash) to conventional naphtha, kerosene, and diesel. Direct use and sale of the FTL to fuel distributors for use as vehicular fuel allows the value of the FTL to be increased by ~28% (Suppes et al, 1998a) and increases the economic viability of Fischer-Tropsch synthetic fuels. The successful use of a C₇ to C₂₄ FTL to power a diesel engine was reported by Suppes et al (1999b).

The C₇ to C₂₄ FTL performed as well as or better than diesel fuel in the modified off-highway test cycle reported by Suppes et. al.. The cetane number of >68 exceeds that of typical FT diesel (also >68). The DD-453T test engine ran without difficulty on the FTL with lower NO_x and particulate matter emissions than #1 diesel fuel at the same conditions. The results of this work identified two possible development obstacles (1) the pour point of FTL is often >-2°C and (2) inclusion of C₁₀₋ fractions in FTL lead to vapor pressures/volatilities exceeding those preferred for diesel fuel.

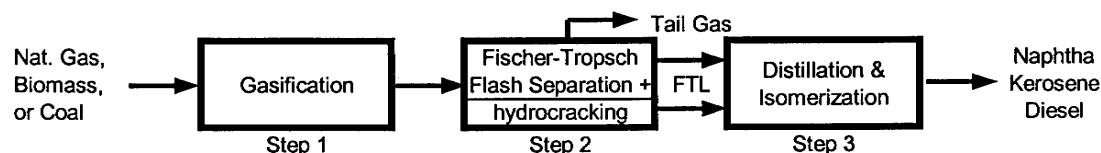


Figure 1. Three step Fischer-Tropsch process with FTL intermediate.

Solutions to pour point problems include (1) use of additives to lower pour points to the -5°C range, (2) blending of FTL with compatible alternatives such as kerosene or naphtha to lower pour points as desired, and (3) limiting use of the fuel to warmer seasons/regions. The combination of these three solutions provide a viable and economical approach.

Solutions to volatility problems reside in restricting applications to those compatible with higher vapor pressures. For many makes and models of vehicles, this may be as simple as educating the users to the fact that the fuel is not diesel fuel and that use of ignition sources (exterior to the vehicle) that were compatible with diesel fuel may not be compatible with FTL. For other applications, the vehicles' fuel delivery systems may need to be changed to ensure that the fuel is not heated excessively as may be allowed with diesel fuel.

Use of formulations with oxygenates further improved performance. For such applications, the FTL would be distributed in pipelines and formulations with oxygenates would be prepared in a manner similar to that done with

gasoline today. Suppes et al demonstrated that mixtures with 25% ethanol can lead to a >60% reduction in particulate matter. Optimal formulations including ~90% FTL, ~10% ethanol, and <1% soybean oil additives (for surfactant and lubricity benefits) were identified. Formulations such as these provide opportunities for those vested in FTL technology (possibly including natural gas, coal, and biomass industries), ethanol, and soybean oil derivatives to work together to develop high performance fuels.

FTL fuels provide an opportunity for a cost competitive and clean-burning fuel to be developed while preserving opportunities for the natural gas, coal, and biomass sectors. These fuels would be clean-burning and can evolve with evolving environmental concerns including the production of these fuels from renewable resources.

REFERENCES

- Suppes, G.J.; J. Terry; M. Burkhart; and M.P. Cupps, "Blends of Fischer-Tropsch Crude-A Lower Cost Route to Diesel Fuel", Fifteenth Annual International Pittsburgh Coal Conference, Pittsburgh, PE, September, 1998a.
- Suppes, G.J.; C.J. Lula; M.L. Burkhart; and J.D. Swearingen. "Performance of FischerTropsch Liquid (FTL) in Modified Off-Highway Diesel Engine Test Cycle" SAE Paper 1999-01-1474, 1998b.

